

# RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

EDITOR

Howard P. Doub, M.D.  
Detroit, Michigan



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## CONTENTS

SOME EXPERIENCES WITH IRRADIATION INJURY. <i>Joseph W. Ferrebee, M.D., and E. Donnell Thomas, M.D.</i>	1
COMPARISON OF THE EFFECTS OF ISOLOGOUS, HOMOLOGOUS, AND HETEROLOGOUS HEMATOPOIETIC TISSUES ON POST-IRRADIATION SURVIVAL. <i>Leon O. Jacobson, M.D., and Eric L. Simmons, Ph.D.</i>	6
THE THEORY AND PRACTICE OF TOTAL-BODY IRRADIATION IN THE DAWN OF THE HOMO-GRAFT ERA. <i>James B. Dealy, Jr., M.D.</i>	11
PHYSICAL CONSIDERATIONS IN THE DESIGN OF FACILITIES FOR THE UNIFORM WHOLE-BODY IRRADIATION OF MAN. <i>Edward W. Webster, Ph.D.</i>	19
CORONARY ARTERIOGRAPHY: DEVELOPMENT OF A METHOD IN ANIMALS WITH PARTICULAR ATTENTION TO PHYSIOLOGIC EFFECTS. <i>Sidney W. Nelson, M.D., William Molnar, M.D., Anthimos Christoforidis, M.D., and Clarence Britt, M.D.</i>	34
SOME FACTORS ALTERING THE SEVERITY OF ACUTE RADIATION PNEUMONITIS: VARIATION WITH CORTISONE, HEPARIN, AND ANTIBIOTICS. <i>William T. Moss, M.D., Francis J. Haddy, M.D., and Sanford K. Sweany, M.D.</i>	50
THE RELATIONSHIP BETWEEN OXYGEN TENSION OF INHALED GAS AND THE SEVERITY OF ACUTE RADIATION PNEUMONITIS. <i>William T. Moss, M.D., and Francis J. Haddy, M.D.</i>	55
INTRACRANIAL POSTERIOR-FOSSA TUMORS. <i>Samuel B. Haveson, M.D.</i>	59
VENTRICULAR SEPTAL DEFECT AND SEVERE PULMONARY HYPERTENSION. RADIOLOGIC CONSIDERATIONS IN SELECTION OF PATIENTS FOR SURGERY. <i>Charles W. Vickers, M.D., Owings W. Kincaid, M.D., James W. DuShane, M.D., and John W. Kirklin, M.D.</i>	69
ANGIOGRAPHY OF THE INTERNAL CAROTID WITH USE OF THE CATHETER TECHNIC. <i>P. Elfvin, M.D.</i>	80
FAULTY CONTRAST INJECTION IN PERCUTANEOUS VENTRICULAR PUNCTURE. <i>Benjamin E. Greenberg, M.D., and Frederick H. Knox, M.D.</i>	85
MICROANGIOGRAPHIC STUDY OF THE VASA VASORUM OF THE THORACIC AORTA. <i>Ayres De Sousa, D.M., and Luiz Alvares, M.D.</i>	91
PHOTOCONDUCTANCE CRYSTALS FOR INTRACAVITARY DOSIMETRY. <i>Emanuel G. Tulskey, M.D., Jen-Ti Chen, M.D., and Arthur Finkelstein, M.D.</i>	98
EXFOLIATIVE CYTOLOGY IN RADIOTHERAPY OF ORAL CANCER. ITS USE IN THE DIAGNOSIS OF RESIDUAL CARCINOMA. <i>W. Umiker, M.D., R. Rapp, M.D., I. Lampe, M.D., and H. B. Latourette, M.D.</i>	107
CALORIMETRIC MEASUREMENTS OF BONE/TISSUE ABSORPTION RATIOS. <i>Paul N. Goodwin, Ph.D.</i>	112
EPISTERNAL BONES. A CASE REPORT. <i>Webster H. Brown, M.D.</i>	116
PULMONARY "COIN" LESION OF UNUSUAL PATHOLOGY. <i>R. Paul, M.D., F.R.F.P.S.</i>	118
WORK IN PROGRESS. THE USE OF VARIDASE DURING RADIATION THERAPY OF HEAD AND NECK TUMORS. <i>Frank Gearing, M.D., Paxton Powers, M.D., and George Cooper, Jr., M.D.</i>	121
NATIONAL COMMITTEE ON RADIATION PROTECTION AND MEASUREMENTS.	122
EDITORIAL: RADIATION AND BORROWED TISSUES. <i>Richard H. Chamberlain, M.D.</i>	123
RADIOTHERAPY IN GREAT BRITAIN. <i>Christian V. Cimmino, M.D.</i>	124
ANNOUNCEMENTS AND BOOK REVIEWS.	125
IN MEMORIAM: DONALD S. CHILDS, M.D.; JOSEPH C. BELL, M.D.	128
RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES.	133
ABSTRACTS OF CURRENT LITERATURE.	138

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Henry Ford Hospital, Detroit 2, Mich.

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## Some Experiences with Irradiation Injury<sup>1</sup>

JOSEPH W. FERREBEE, M.D., and E. DONNALL THOMAS, M.D.

THE FOLLOWING is a brief review of current experiences with the treatment of the marrow injury that follows whole-body irradiation in man. The studies described are essentially those made with colleagues at the Mary Imogene Bassett Hospital, Cooperstown, New York: Dr. Otto Sahler, Radiologist; Dr. Joe Cannon, Pediatrician; Dr. Charles Ashley, Pathologist; Drs. H. L. Lochte, Jr., John A. Mannick, Emery Herman, William Greenough, Edward Hager, and Major T. W. Richey, U. S. Air Force, Research Associates. For a starting point this group has used the classical work on marrow replacement and marrow transplantation as extensively explored in irradiated rodents (1). As pilot for its own studies it has used the dog, an animal in which the treatment of post-irradiation marrow injury appears to offer difficulties comparable to those encountered in man (2, 3). The patients observed have been those with leukemia who received whole-body irradiation as part of their therapy. Doses have been 150 to 1,500 r measured in air at midbody position. Exposures have been at 2 to 2.5 meters target-to-source distance, with a pair of symmetrically placed cobalt-60 units, one on either side of the patient at rest in bed. Dose rates have been 30 to 40 r per hour. Administration

has been essentially continuous; thus about forty-five hours have been required for an exposure totaling 1,500 r.

Figure 1 shows a dog three months after an exposure of 750 r. The animal is quite well. He received no infusion of marrow but was given fresh blood and antibiotics daily until his own marrow regenerated, about five weeks after exposure. This type of recovery from radiation injury presupposes a long and hazardous period of marrow aplasia and meticulous supportive therapy, for a month at least. The dog is from a series recently studied, with us, by Major T. W. Richey of the U. S. Air Force.

A child receiving an exposure of 1,000 r. was isolated and given antibiotics and fresh blood. In the two weeks following irradiation, seven infusions totaling several billion fetal hematopoietic cells<sup>2</sup> were administered. Since no evidence of marrow function appeared in three weeks, several billion fresh adult marrow cells were taken from one of the patient's relatives and infused on the twenty-third day after irradiation. Evidence of returning marrow function appeared on the thirty-second day, that is, white cells, particularly polymorphonuclear leukocytes, appeared in the circulation at that time. However, immunologic analysis of the erythrocytes

<sup>1</sup> From the Mary Imogene Bassett Hospital (J. W. F., Research Physician; E. D. T., Physician-in-Chief), Cooperstown, N. Y. Presented as part of a Panel Discussion on Bone Marrow Transplants and the General Immunological Problems, at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15-20, 1959.

The data presented were obtained with the support of Atomic Energy Commission Contract AT (30-1)-2005, United States Public Health Service Grant A2215, and a Grant from the John A. Hartford Foundation.

<sup>2</sup> Supplied by Dr. H. E. M. Kay, of the Royal Marsden Hospital, London.



Fig. 1. Dog three months after exposure to 750 r. Autogenous recovery of marrow function.

produced indicated that this marrow function was essentially a regeneration of the patient's own marrow and not an engraftment of the infused fetal or adult hematopoietic tissues.

These observations demonstrate that exposures to radiation commonly accepted as lethal need not be so if the patient is properly cared for. Marrow will regenerate from remnants not completely destroyed by radiation at these doses, namely, 800 to 1,000 r, provided the patient is kept alive long enough by appropriate supportive treatment, chiefly fresh blood and antibiotics, and is isolated to reduce the possibility of death from intercurrent infectious disease. How often this can be done successfully is not known, but it obviously has been done and therefore can be done.

Figure 2 shows several dogs from a series studied, with us, by Dr. John A. Mannick last year (4). The picture was taken nine to ten months after exposures of 1,000 to 1,500 r. These dogs received infusions of small seed samples of their own marrow

shortly after irradiation. Marrow was removed from a femur and set aside. The dog was irradiated. \* The marrow samples, 2 or 3 billion cells, were re-infused. This treatment, re-infusion of autologous marrow, appears quite satisfactory. The dogs are given antibiotics and occasionally receive transfusions in the first week following irradiation, but they rarely appear critically ill and marrow function usually returns in two weeks instead of in the four or five weeks that are required for an autogenous regeneration from surviving remnants. In several of the dogs shown the seed sample of marrow had been stored at  $-80^{\circ}\text{C}$ . in glycerol. The time limits of this type of useful storage of marrow are not known but are presumably measured in months or years (5).

A little girl, one of identical twins, was exposed to 900 r of whole-body irradiation as part of her treatment for acute leukemia. This patient was not particularly ill after irradiation. An infusion of marrow from her twin induced a return of function in two weeks. Similar studies in twins have been completed with exposures of 1,200 (6) and 1,600 r (7).

Recovery appears to be induced in man after infusion of isologous marrow from an identical twin just as it is easily induced in dogs by infusion of autologous samples of seed marrow. The problem with most of our patients is that they do not have preserved samples of normal marrow of their own set aside as seed prior to therapy. Dr. N. B. Kurnick, however, has made studies of patients receiving almost complete whole-body irradiation in whom it has been possible to set aside, frozen in glycerol, a small seed sample of essentially normal marrow prior to radiotherapy. Dr. Kurnick and Drs. Newton and Humble and their colleagues of London, who have made similar studies, have evidence that the injection of an autologous seed sample accelerates the rate of return of normal marrow function in their heavily irradiated patients (8, 9).

Figure 3 shows another dog in Dr. Mannick's series. The picture was taken



Fig. 2. Dogs nine to ten months after exposure to 1,000 to 1,500 r. Recovery of marrow function following infusion of autologous marrow removed prior to irradiation.

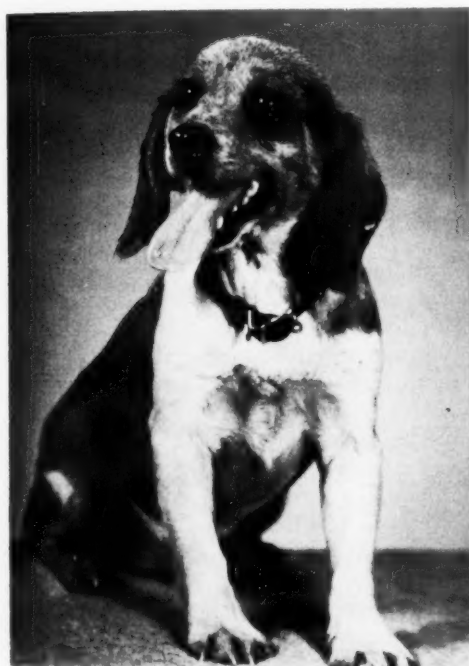


Fig. 3. Dog eight months after exposure to 1,800 r and infusion of marrow from another dog. Recovery of marrow function following infusion of homologous marrow.



Fig. 4. Unrelated dogs six weeks after male on left was exposed to 1,300 r and given a marrow transplant and an effective kidney transplant from the female on the right. Recovery of marrow function following infusion of homologous marrow.

eight months after three exposures of 600 r given on successive days for a total of 1,800 r. The dog received marrow from a female and his leukocytes still have the female sex tag. The dog is alive and well.

Lymph node function in this animal on biopsy appeared partially restored within three months after irradiation. The dog has now been off all antibiotics and hyper-immune sera for several months, and one



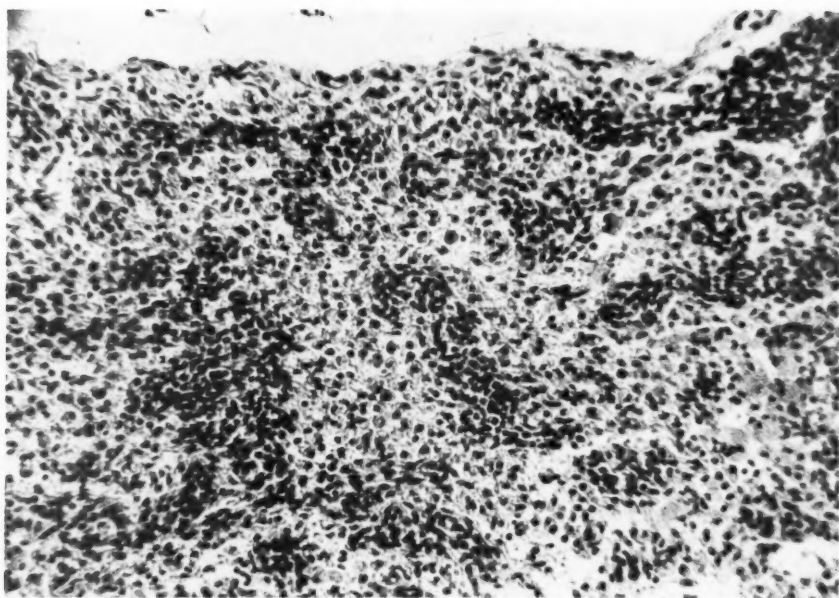


Fig. 5. Section of lymph node from male dog of Fig. 4, seventy-five days after irradiation and sixty-five days after successful marrow transplantation. Little evidence of regeneration of lymphoid tissue.

presumes that in this radiation chimera lymph-node structure and immunologic defenses are fully restored. These points are now being tested.

Figure 4 shows two dogs, with Dr. John A. Mannick, the surgeon who did the work (10). The dog on the left received 1,300 r, a marrow graft, and then a kidney graft from the female on the right. Marrow function returned in two weeks. The engrafted homologous kidney functioned normally within two weeks of its insertion. When this picture was taken, the dog's own kidneys had been removed for several weeks. The animal died of pneumonia on the seventy-fifth day, with normal blood urea and electrolyte levels and with a normal appearing bone marrow. Figure 5 shows the basic trouble in this instance. Lymph-node histology and function had not been restored. Supportive treatment and isolation were inadequate, and death occurred as a result of intercurrent infectious disease.

One of the essential problems in homologous transfers of marrow after irradiation

is proper restoration of lymph-node function (11). This appears true in all species, including rodents, and is related to the graft *vs.* host reaction, that is a reaction of the foreign lymphoid tissue included in the marrow infusion against the host's tissue antigens, primarily at the home sites of the transplanted lymphoid cells in the lymph nodes and spleen. Adaptation or adjustment of this reaction will occur if the animal is protected from intercurrent disease during the two or three months that are required for the adjustment to take place.

We have no patient with a successful permanent graft of homologous marrow after irradiation, nothing to match the results shown in dogs, and apparently no one else has (12). One or two patients after infusions of homologous marrow have shown signs of early but temporary marrow function of graft origin (13). Dr. Mathé has also had evidence of partial but temporary function in marrow grafts in several patients (14, 12). Here we are speaking of homologous marrow grafts,

i.e., grafts of marrow from other persons, not of marrow grafts from an identical twin and not of re-infusions of the patient's own marrow. These latter, isologous and autologous grafts, work well.

We have speculated on the difficulty of securing successful permanent homografts of marrow in man and have wondered why it has been difficult to get good homologous grafts of marrow in dogs routinely. Lately we seem to be securing results in dogs using radiation in doses greater than those just discussed, that is, up to 2,000 r. Perhaps radiation dose is also the problem in man. It may be that in both man and dogs homologous marrow is readily accepted only after exposures considerably greater than those customarily successful in rodents. Our present studies are along these lines, and we are increasing our doses progressively. So far we have not found intestinal damage necessarily fatal in dogs after 1,800 r administered at 18 r per minute (15). Perhaps the use of antibiotics has controlled one aspect of the intestinal syndrome, the systemic invasion by intestinal bacteria. Perhaps the intestines of men and of healthy dogs are more resistant to radiation than hitherto supposed. Perhaps the supportive treatment used, fluids and transfusions, has been more adequate. In any event, the acquisition of further data on these subjects and on radiation effects in general, in men and in dogs, would appear most desirable. Fortunately it would also appear that such data can be obtained. For example, the data on patients that have been presented came from studies in which the welfare of the individual studied was kept securely in mind and in some instances significant clinical improvement was obtained.

Mary Imogene Bassett Hospital  
Cooperstown, N. Y.

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(Pro le summario in interlingua, vider le pagina 10)

# Comparison of the Effects of Isologous, Homologous, and Heterologous Hematopoietic Tissues on Post-Irradiation Survival<sup>1</sup>

LEON O. JACOBSON, M.D., and ERIC L. SIMMONS, Ph.D.

THROUGH the centuries man has yearned for the possibility of exchanging new parts for old, of removing a damaged or diseased portion of his body and transplanting in its stead a healthy substitute. In the early days many daring attempts were made at such transplantation, even to the extent of using tissues from animals. Gibson (1) has reported from the year 1682 one of the earliest of such attempts on record, on a nobleman who had suffered a skull fracture on the battlefield. An enterprising surgeon used a piece of the skull of a dog to repair the damage, and the warrior lived. Indeed, so proud was he of this unique addition to his anatomy that he made the mistake of telling his friends about the operation and the news eventually reached the ears of the officials of the Church. They promptly ruled that no good Christian should have part of an animal within his body and so ordered it removed.

This anecdote serves as an introduction to our discussion, for amazing strides in the knowledge of radiation and its biologic effects have been made since the development of the atomic bomb and the dawn of the atomic age. Already research in the field of radiation biology and medicine has brought into view new horizons with far-reaching possibilities of effecting cures, contributing to a better understanding of the basic principles of the immune mechanism, and indeed opening up the possibility of tissue and organ transplantations.

Even ten years ago no treatment for post-irradiation damage was known, despite the fact that Roentgen discovered x-rays in 1895 and that they have been in use ever since. Once the damage was done, once the

rays had delivered their undiluted physical impact on the living system, no restorative treatment was available which could reverse their lethal action. It was known, to be sure, that one could modify the biologic action of irradiation by pre-irradiation treatment. Treadwell and Gardner (2), for example, working at Yale, as far back as 1938 showed that when estrogens were given to mice ten days before irradiation the animals were able to survive dosages well above the lethal range. And, in the late 1940's, Barron (3), Patt (4), and Cronkite (5) showed that the sulfhydryl compounds, such as glutathione and cysteine, would protect, provided they were present when the ionizing radiations penetrated the body.

It was at about this time that we had the good fortune to be exploring the effect of lead protection of the spleen on regeneration of blood-forming tissues following total-body irradiation and realized that this procedure prevented radiation mortality despite the administration of lethal dosages. Not only did the spleen itself hypertrophy and prevent the characteristic fatal depression in blood elements, but spleen shielding was accompanied by rapid regeneration of the bone marrow which but a short time previously had been depopulated. We soon explored other protective treatments, such as transplantation of spleens of new born mice and intravenous injection of homogenates of spleen and embryo liver, and found that mice thus treated would live even though they had been irradiated with dosages well above the lethal range (6-8). Our colleague, the late Egon Lorenz (9), expanded the list of hematopoietic tissues having post-

<sup>1</sup> From the Argonne Cancer Research Hospital (operated by the University of Chicago for the U. S. Atomic Energy Commission) and the Department of Medicine, University of Chicago, Chicago, Ill. Presented as part of a Panel Discussion on Bone Marrow Transplants and the General Immunological Problems, at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15-20, 1959.



irradiation protective ability, with his finding that bone-marrow cells are also effective. Thus, it soon became apparent that following administration of a lethal dose of irradiation, twenty-eight-day survival could be enhanced dramatically by injections of a variety of blood-forming cells, including combinations as genetically distinct as guinea-pig or rat cells in irradiated mice.

It was only natural that the mechanism responsible for this recovery should intrigue us and that many possible explanations should be suggested. It seemed possible that the addition of normal healthy cells detoxified some unknown poison produced in irradiated tissue, that there was seeding by the introduced cells, or that some humoral substance which hastened the recovery of the damaged tissues in the animal's own body was released by the transplanted cells. While it was impossible to identify the mechanism on the basis of the facts available during these early years, it is true that we leaned in favor of the humoral hypothesis because it seemed inconceivable that cells from a rat could live in the body of a mouse without being rejected. We shall see how the clever approaches of many additional workers exploring this field made possible the solution of the problem.

From the outset it was obvious that isologous tissues, that is, tissues from the same inbred strain, would provide excellent long-term survival against irradiation death from dosages often as high as twice the LD 50. However, in 1954 a new phenomenon was observed that was to be of extreme importance in setting the stage for the realization that injected cells actually colonize their weakened host. Barnes and Loutit (10) discovered that when hematopoietic cells from a different strain or species were used for post-irradiation protection, even though excellent survival followed the acute radiation crisis, the animals worsened and slowly succumbed by one hundred and twenty days to what came to be referred to as "secondary disease" or "homologous disease." These

observations provoked a strong suspicion that a severe immune interaction was involved, and that the grafted cells were either attacking their host or *vice versa*. Indeed, while there is now no doubt that an immunologic reaction is going on, the controversy still rages as to who is attacking whom.

There now followed the magnificent demonstration by three independent groups of workers that the transplanted cells indeed persisted and recolonized the irradiation-weakened host animal. Lindsley *et al.* (11) at Oak Ridge showed, by the use of appropriate antisera, that the circulating erythrocytes present in the surviving irradiated injected animal had the same immunologic pattern as did those of the animals whose bone marrow was used for the injection. Hence, these must be descendants of the injected bone marrow cells. Meanwhile, Nowell, Cole, *et al.* (12), in San Francisco, used histochemical methods to show that if a mouse were given rat marrow after lethal irradiation, the marrow in the mouse's body would, following its recovery, stain with alkaline phosphatase in a manner characteristic of the rat. Finally, the work of Ford, Hamerton, Barnes, and Loutit (13), in England, removed any doubts remaining that the injected cells were transferring their behavior pattern to their new host and proved conclusively that the colonizing cells were the descendants of the injected stem cells. They transplanted marrow from other mice, using a chromosomal abnormality as a genetic marker, and found that the regenerating tissues in the irradiated mouse contained these abnormal chromosomes.

We are often asked why we didn't realize during those early years that our radiation survival was due to repopulation; why we didn't give it more serious thought. We were certainly aware of the tremendous background of literature on the effect of radiation on the immune response, some of this work in fact, such as Hektoen's, going back to the early 1900's. We knew, of course, that if one gave low doses of irradiation to an animal and then chal-

lenged with a foreign antigen, the animal was no longer able to form antibodies against the antigen during the early period, but that, as it recovered, its immune production mechanism also recovered. And, of course, no one had ever tried to challenge an animal following a supra-lethal dose of irradiation because one cannot do an immunological experiment on a dead horse, and at that time there was no way to save the life of a lethally irradiated animal.

Thus, changes in the immune response became the key to an understanding of factors at work in post-irradiation survival, and many dramatic experiments that were performed about this time developed these concepts. A review of the irradiation studies of the period would not be complete without mention of the exciting transplantation experiments in which Main and Prehn (14) were able to circumvent the homograft reaction. After giving 800 r to DBA/2 mice followed by supportive injections of BALB/c bone-marrow cells, they found that surviving mice retained a skin graft from mice of the strain used as the source of the bone marrow. Normally, of course, such a transplant between strains is rejected. A great deal of work has since been done on experimental tumors to explore this host-graft mechanism.

Our realization of the fact that supra-lethal doses of irradiation paralyzed the immune processes of the body, and thus allowed the growth of foreign transplanted cells, has in recent years been reinforced by the basic immunologic research of such workers as Billingham, Brent, and Medawar (15) and many others. Their work has shown that one can inject an embryo, or in some cases the newborn, with foreign antigens during the stage of antibody inactivity. Such an individual will then develop a tolerance to the injected antigens and will thereafter not form antibodies against it. The supralethally irradiated animal is apparently very much like the embryo, in the sense that it is not capable of antibody formation at the time

the foreign cells are injected and some degree of tolerance is developed. In the present state of our knowledge, it is difficult to be certain where we stand in making assumptions about transferring our research findings from the mouse to practical applications in man. This is well illustrated by Drs. Ferrebee, Webster, and Dealy, the other participants in this symposium. The picture is not all black and white at the moment, even in studies with mice, for sometimes irradiated mice injected with homologous bone marrow will live out their remaining life span with a permanent transplant, while at other times the foreign tissues seem to be rejected and the mouse reverts to its original tissues.

We have come a long way, but there are still many promising leads to be explored. Experiments with animals suggest that the use of embryonic tissues rather than of adult bone marrow will also lead to the development of tolerance and that fewer secondary immunologic complications may develop when the irradiated animal is colonized by descendants of such embryonic cells. While this has not yet been shown to be true in man in preliminary experiments using fetal materials, as has been pointed out by Ferrebee, it has yet to be tested in greater detail.

Another avenue of approach which some workers are already exploring is the possibility of suppressives which operate somewhat as follows: Suppose that bone marrow from mouse B when injected into mouse A leads to severe secondary disease. Now, if it were possible to find suppressor substances that would so alter the immune behavior pattern that permanent tolerance would result, then there would be no secondary immune interaction. Some success in this direction has already been achieved by Beilby and colleagues (16), even though this approach is as yet only in the introductory experimental stage. They have reported the case of a patient with Hodgkin's disease who suffered from acute bone-marrow failure due to chemotherapy. This they treated with a bone-marrow trans-

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fusion from her sister. The bone-marrow graft has now survived for more than six months and is leading to the production of an ever increasing proportion of the patient's erythrocytes.

One last point that might be mentioned is the possibility that even homologous cells may somehow, by their temporary presence, aid the regeneration of the irradiated recipient's own cells, which would thus be restored to normal life. As reported by Mathé (17), the bone-marrow transfusions from French volunteers that were recently given to the accidentally irradiated Yugoslav scientists may possibly represent such an instance for, following the recovery of their peripheral blood elements, the donor cells are no longer present. In experiments with rabbits, injections of mouse cells increased survival but did not lead to colonization, and indeed even such nonspecific irritants as ground glass have been shown to stimulate the animal's own regeneration and hence aid in radiation survival.

In conclusion, it may be felt that we have not yet come through with anything very practical for application to the human being. But at least in these last few years we have asked ourselves a great many questions, and I suspect have provided the radiologists with thousands of projects for exploration in the next ten years.

Argonne Cancer Research Hospital  
950 E. 59th St.  
Chicago 37, Ill.

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#### SUMMARIO IN INTERLINGUA

Comparation de Tissus Hematopoietic Isologe, Homologe, e Heterologe in Lor Effectos Super le Surviventia Post Irradiation

Es revistate studios experimental relative al effectos de transplantate tissus hematopoietic super le surviventia post irradiation. Ab le initio il esseva evidente

que un eccellente surviventia a longe duration poteva esser effectuate in fortemente irradiate animales (recipiente usque a duo vices le dose letal median) per le injection

de tissu ab le mesme (endogame) racia (i. e. tissu isologe). Tamen, cellulas ab un altere racia o ab un altere specie, ben que illos manteneva le animal durante le crise acute de radiation, non prolongava le vita in ultra de cento e vinti dies. Incompatibilitate se manifestava e le morte superveniva.

Investigationes additional monstrava que le implantate cellulas alien persisteva e re-formava colonias in le irradiate hospite, lo que indica que le processus immunologic del corpore habeva essite paralyse per le irradiation. Esseva trovate in certe casos que le uso de fetal tissu hematopoietic reduceva le complicationes immuno-

logic secundari e obviava le latente incompatibilitate alteremente observate in transplantationes homo- e heterologe. Iste phenomeno ha non ancora essite demonstrate in humanos, sed studios currentemente in progresso investiga le uso possibile de substantias suppressori capace a alterar le comportamento immunologic de tal maniera que un tolerantia permanente resultarea.

Es mentionate le possibilitate que mesmo cellulas homologue es capace—in un maniera o un altere—a promover per lor presentia temporari le regeneration del cellulas autochthone in le recipiente del irradiation.

#### SUMMARIO IN INTERLINGUA

#### Experientias con Lesiones de Irradiation

(Pagina 1)

Es reportate studios experimental in canes e observationes in un numero de patientes leucemic qui recipeva irradiation del corpore total como parte de lor therapia. Le presentation se face ab le puncto de vista del lesiones de irradiation.

Un can subicite a 750 r se restabliava post administrationes diurne de sanguine fresc e de antibioticos, continuate usque al regeneration del medulla ossee circa cinque septimanas post le exposition. Un patiente pediatric recipeva le mesme tractamento, sed con le addition de septe infusiones de un total de plure milliardos de fetal cellulas hematopoietic e subsequentemente de plure milliardos de adulte cellulas fresc ab un consanguineo. Signos de un retorno del function del medulla ossee sequeva iste tractamento.

In canes, restablimento sequeva etiam le infusion de micre specimens seminal de medulla obtenite ab le animales mesme e re-administrate brevemente post le irradiation, durante que in humanos le infusion de medulla isologe ab un gemino identic resultava in le restauration functional.

Un del associate problemas in transplantationes homologue de medulla post irradiation es le restauration del function del nodos lymphatic. Isto require le protection contra omne maladia intermittente durante duo o tres menses.

Nulle permanentemente successose grafos de medulla homologue esseva obtenite in humanos. Es presentate le hypothese que grafos homologue esserea acceptate plus prestemente post irradiation in doses plus alte que illos usate usque al presente.



## The Theory and Practice of Total-Body Irradiation in the Dawn of the Homograft Era

JAMES B. DEALY, JR., M.D.

THE administration of total-body radiation as a prelude to the transplantation of tissues between genetically unrelated individuals may be approached from two theoretical standpoints, which share the common objective of altering normal antibody response.

On the one hand, doses of radiation in the potentially lethal range may be employed in the expectation that infused bone marrow, by its functional replacement of the recipient's marrow, will provide effective support through the acute radiation syndrome. This successfully "grafted" marrow, as the recipient's new immunological recognition system, should then be tolerant of other tissues grafted from the same or genetically identical donors.

Alternatively, total-body irradiation, from which spontaneous regeneration of host marrow may be predicted, cannot be excluded as having a sufficiently suppressive effect on lymphopoietic and reticulo-endothelial elements to permit of a period of immunologic impotence. If there is an analogy between this state and the perinatal state of immunologic immaturity (1), during which tolerance to homologous (same species but genetically unrelated individuals) tissue antigens can be acquired, it is not irrational to hope that the stage is set for the operation of similar mechanisms during the post-irradiation period.

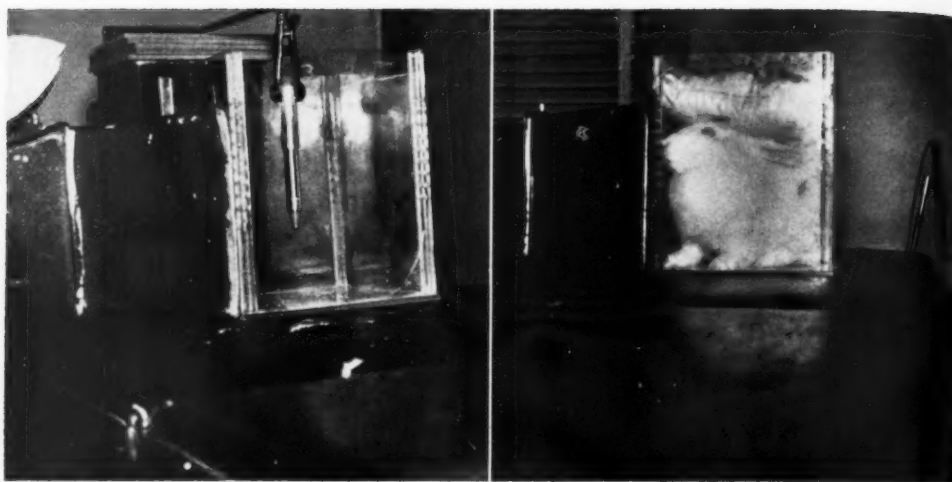
The difference between these two approaches may be a predominantly quantitative one. In the adoption of the high-dose pathway, with an apparent immunologic default on the part of the host, one must consider whether success depends *per se* upon eradication and complete replacement of the lymphopoietic-reticulo-

endothelial system. Irradiation chimeras have been shown to have either hematopoietic cells or immunologic responses that are unique to the original identities of both recipient and donor (2-6). The implication, therefore, is that a continuing degree of host marrow and reticulo-endothelial proliferation can be expected even after the doses of irradiation that are required for the acceptance of marrow. The unsuccessful attempts to destroy human leukemia may be cases in point (7, 8).

The desirability of pursuing the low-dose approach, with its major circumvention of the difficult and taxing problems of the management of the acute radiation syndrome, is obvious. However, even though the theoretical difference may be quantitative, the fact remains that the best chances of promoting tolerance to fixed tissue currently appear to reside in the previous or parallel acceptance of a true bone-marrow homograft. In order to obtain this, the potentially lethal doses of radiation, which will produce the greatest net depression in the ratio between new, unmodified antibody and antigen, have a demonstrated superiority.

Our experience thus far has shown that the best homologous bone-marrow protection against 250-kv whole-body irradiation in the rabbit is achieved following a total dose of 1,100 r, given in successive daily doses of 600 and 500 r. Within a matter of hours after the second exposure, of the order of 2 billion nucleated marrow cells from a genetically unrelated weanling donor are infused intravenously and a full-thickness skin graft is transferred from the marrow donor to the irradiated animal's ear. In certain instances, marrow has been pooled from multiple (five)

<sup>1</sup> From the Department of Radiology of the Harvard Medical School at the Peter Bent Brigham Hospital, Boston, Mass. Presented as part of a Panel on Bone Marrow Transplants and the General Immunological Problems, at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15-20, 1959.



Figs. 1 and 2. Lucite animal-irradiation container with ionization chamber at center of irradiated volume. Rabbit undergoing whole-body irradiation.

donors, in which event skin is grafted from each of the donors to the pool. The details of this procedure have been reported previously (9, 10).

Radiation dose is expressed as air dose at the center of the irradiated volume (Fig. 1). At each session, the total dose is

TABLE I: LETHALITY OF EXPERIMENTAL PROCEDURES

	No.	Per Cent of Group
Animals surviving irradiation	143/153	94
Animals surviving marrow infusion with and without skin grafting	83/96	86

divided evenly among four portals in the axis of two body planes. On the basis of Masonite phantom measurements which simulate the irradiated volume adjusted by rice bolus to 20 c.c. (Fig. 2), mid-plane homogeneity is in the range of  $\pm 5$  per cent, with the absorbed dose at the center of the animal approximately 1,000 rads. Under these experimental conditions, this dose has an LD 89 in two weeks.

A certain immediate attrition results from the irradiation itself. As shown in Table I, 10 of 153 animals succumbed either between the two doses or immediately after the second, for an overall sur-

vival of 94 per cent. Similarly, there is a mortality associated with the marrow infusion and skin-grafting procedures. Among 96 animals subjected to these events, there were 13 deaths, 8 of which were attributed to anesthesia and 5 to marrow emboli. The latter hazard can be reduced effectively by techniques designed to diminish particle size and fat content.

The degree of protection afforded by bone marrow, if the animal survives the irradiation and immediate post-irradiation procedures, is shown in Table II.

TABLE II: PERIODIC SURVIVAL OF ANIMALS TOLERATING EXPERIMENTAL PROCEDURES

	No.	>2 Weeks (%)	>4 Weeks (%)	>7 Weeks (%)
X-ray controls	47	11	9	6
X-ray and marrow	83	86	49	37

The baseline periodic survival of the irradiated but untreated animals is seen to be 11 per cent beyond two weeks, 9 per cent beyond four weeks, and 6 per cent beyond seven weeks. The figures given for the animals receiving marrow are all-inclusive and do not take into account whether the marrow is from single or multiple donors or whether or not a proliferating homograft was achieved. The latter, of

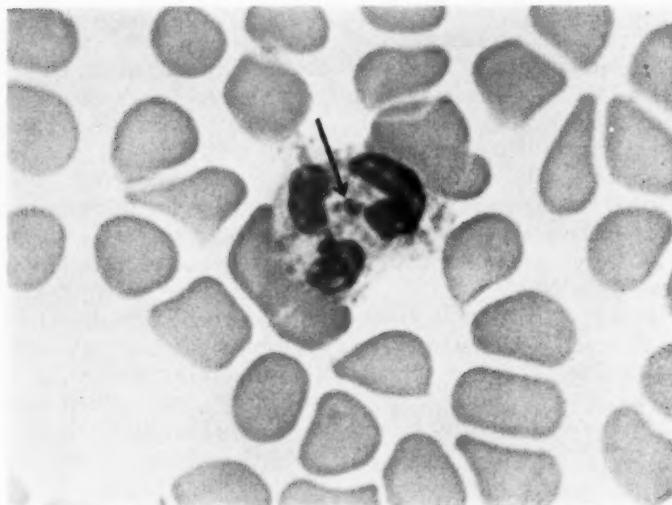


Fig. 3. Female leukocyte showing characteristic drumstick or chromatid tag projecting from lobe of adult polymorphonuclear neutrophil.

course, is an important consideration. To what extent does the acceptance of marrow as a graft augment protection?

TABLE III: PERIODIC SURVIVAL AS A FUNCTION OF MARROW TAKE

	No.	>2 Weeks (%)	>4 Weeks (%)	>7 Weeks (%)
Successful marrow homograft				
Single donor recipients	45	100	64	51
Pooled marrow recipients	22	73	27	14
Total	67	91	52	39
Unsuccessful marrow homograft				
Single donor recipients	6	83	50	33
Pooled marrow recipients	10	50	30	30
Total	16	63	38	31

Table III shows the periodic survival as a function of marrow take. It is apparent that the proliferation of infused marrow contributes something over and above nonspecific support. This is to be expected, since the existence of a substitutive immunological competence during the post-irradiation period of maximum vulnerability to infection is clearly advantageous. It is equally apparent, however, that the salutary influence of the proliferating, grafted marrow is neutralized with the passage of time, particularly in the pooled marrow group, which involves a more complex set of immunologic reactions.

Very possibly a reverse immunologic situation, in which the unwitting graft reacts against the host, may achieve such proportions that it becomes lethal to the recipient.

The fact that the numbers in the unsuccessful marrow graft category are small is merely a commentary on the efficacy of the dose. In other words, there appears to be a range of radiation dose in which at least short-term survival tends to be equilibrated with a successful marrow homograft. At 1,100 r, the chances of obtaining a take following infusion of homologous marrow from a single donor are 88 per cent. Although efforts have been unsuccessful thus far, it is entirely possible that higher doses, on a different protraction schedule than has been employed, might make a successful graft and survival synonymous. The fear of a countermanding supralethal radiation effect is somewhat belied by the fact that very large doses of whole body irradiation in the dog can be protected against by the use of autologous marrow (11). Thus, mortality from large doses of x-rays cannot be divorced entirely from immunologic, host-versus-graft considerations in homologous systems.

The assessment of a proliferating marrow homograft in these experiments depends upon the identification of donor female leukocytes in the peripheral blood of the irradiated male recipient (Fig. 3). The results, therefore, permit conclusions only with respect to a take in the white cell series and shed no light on any augmentation of tolerance that might be attendant upon a concomitant proliferation of donor erythropoietic cells.

Correlation between successful bone-marrow (white-cell) grafts and skin grafts is shown in Table IV. The two animals

TABLE IV: CORRELATION BETWEEN CIRCULATING FEMALE WBC AND SKIN GRAFT SURVIVAL IN ANIMALS LIVING LONGER THAN TWO WEEKS

Recipients	Number of Animals				
	♀ WBC Present	♀ WBC Absent	Skin Graft Acceptance	Skin Graft Rejection	Skin Graft Inconclusive
Single donor marrow	10	0	10	0	0
Pooled marrow	16	5	16*	3†	2‡

\* 57 grafts accepted by 16 animals.

† 15 grafts rejected by 3 animals.

‡ 5 of 10 grafts intact at death on fifteenth day.

of inconclusive graft status died on the fifteenth day with an aggregate of 5 out of 10 grafts intact, but without having shown evidence of marrow proliferation. Since the average rejection time for grafts in irradiated controls not receiving marrow and in irradiated animals that do not accept marrow is approximately twenty-three days, the retention of skin grafts for this period need not necessarily be considered a dichotomous result—particularly since the remaining animals fell into two distinct patterns. Of these remaining rabbits, no animal accepted skin that did not accept bone marrow and, conversely, every animal that accepted marrow accepted skin from either its single marrow donor or from one or more donors to its marrow pool.

This, then, was the experimental background of a human application which was prompted by the presentation of 2 patients whose solitary kidneys had been removed following rupture. These patients appear as numbers 1 and 2 in Tables V and VI,

along with the 4 additional patients who comprise our total experience in man to date. Since most of these cases will be reported in detail elsewhere, only salient, summary features are included here.

The initial attempts involved the use of large, single doses of 2-Mev radiation<sup>2</sup> followed by the infusion of bone marrow. In one patient (GL), 107 billion marrow cells were pooled from 17 donors, including a small percentage from a 4-year-old hydrocephalic female whose kidney was transplanted four days after irradiation. For the other patient, a twelve-year-old boy (NW), 10.5 billion marrow cells were taken exclusively from his mother as the potential kidney donor. Because of the general deterioration of his condition, however, it was not deemed justifiable to sacrifice one of the mother's kidneys, and no renal homograft was carried out. In neither patient was there any conclusive evidence of a marrow take, and both died as a result of hemorrhage and infection. At autopsy of the first patient thirty-two days after irradiation, there were no morphologic evidences of a rejection pattern in the kidney that had been transplanted.

The failure to achieve effective control of sepsis and hemorrhage through marrow support in these patients tempered any enthusiasm for proceeding to higher dose levels, not because theoretical justification was lacking, but because the uncertainties of gauging the optimal dose were felt to be too great when dealing with the more elective situation of advanced renal disease. Accordingly, the remaining 4 patients were given doses of radiation designed to produce marked but not irreversible bone-marrow depression.

The first of these patients was a 23-year-old chronically uremic white male (JR) whose kidney donor was a dizygotic twin brother with 26 compatible blood groups. The lack of identity was corroborated by the repeated rejection, by the healthy sibling, of skin transferred from

<sup>2</sup> Irradiation carried out by Dr. Joseph H. Marks at the New England Deaconess Hospital.



TABLE V: TOTAL-BODY IRRADIATION: SUMMARY OF HUMAN EXPERIENCE: I

Patient and Age	Diagnosis	Nominal Air Dose (r)	Kidney Source	Marrow Source	Survival After X-ray	Cause of Death	Kidney Rejection
1. GL 31	No kidneys	600	Indifferent 4-year-old female	Pooled (17 donors)	32 days	Hemorrhage and infection	0
2. NW 12	No kidneys	700	...	Mother	25 days	Hemorrhage and infection	...
3. JR 23	Chronic glomerulonephritis	250 and 200	Fraternal twin	...	10 mo.	...	?
4. RD 56	Subacute glomerulonephritis	250 and 200	Indifferent 6-year-old male	...	19 days	Uremia	Cortical necrosis (major blood incompatibility)
5. MC 15	Chronic glomerulonephritis	250 and 150	Father	...	22 days	Hemorrhage and infection	0
6. GC 20	Chronic glomerulonephritis	250	...	...	18 days	Uremia	...

TABLE VI: TOTAL-BODY IRRADIATION: SUMMARY OF HUMAN EXPERIENCE: II

Patient	Dose (r)	Source and h.v.l.	—Maximum Retic.	Depression of WBC	Platelets	Gastrointestinal Symptoms	Central Nervous System Symptoms
1. GL	600	2 Mev;/7.3 mm. Pb*	0 48 hr.	200 1 wk.	20,000 2 wk.	Early nausea and vomiting; bloody diarrhea	Seizures; ? diuresis
2. NW	700	2 Mev;/7.3 mm. Pb	0 1 wk.	250 2 wk.	0 2 wk.	Esophagitis; bloody diarrhea	...
3. JR	450	250 kv/3.0 mm. Cu†	0.2 2 wk.	0 3 wk.	55,000 2 wk.	Stomatitis; parotitis	...
4. RD	450	250 kv/3.0 mm. Cu	0.5 2 wk.	1800 2 wk.	57,000 10 days	...	...
5. MC	400	250 kv/3.0 mm. Cu	0 2 wk.	50 2 wk.	1,000 2 wk.	Parotitis	Seizures (drug intoxication)
6. GC	250	250 kv/3.0 mm. Cu	1.0 10 days	3000 1 wk.	100,000 2 wk.	Parotitis	Seizures (drug intoxication)

\* Average dose rate of 3 r/min. at distance of 19 feet.

† Average dose rate of 5.5 r/min. at distances of 150 to 160 cm.

the sick twin. As can be seen in Table VI, the dose of radiation administered achieved the desired marrow depression, but permitted spontaneous recovery in the presence of a promptly functional renal homograft. It is noteworthy that in this patient, the correction of uremia and the surgical removal of his own infected kidneys coincided with the reversal of the hematologic picture. At this report, some ten months after transplantation, the patient remains well clinically (Fig. 4), although findings in his urinary sediment suggest that early rejection processes may be operative. With close consanguinity between recipient and donor, the contributory role of radiation to the develop-

ment of prolonged, partial tolerance is documented by this ominous development.

From the hematologic responses of the remaining 3 patients, it can be seen that, although they are dose-dependent, there is a distinct individual variation. Because of an early decline in white count and platelets, the second dose of radiation in patient No. 5 (MC) was reduced to 150 r but, notwithstanding, hemorrhage and infection were important contributory causes to her demise. The second dose of radiation in patient No. 6 (GC) was omitted when her potential kidney donor had to be disqualified for medical reasons.

Since the objective in the last 4 patients was modification of the immunologic speci-

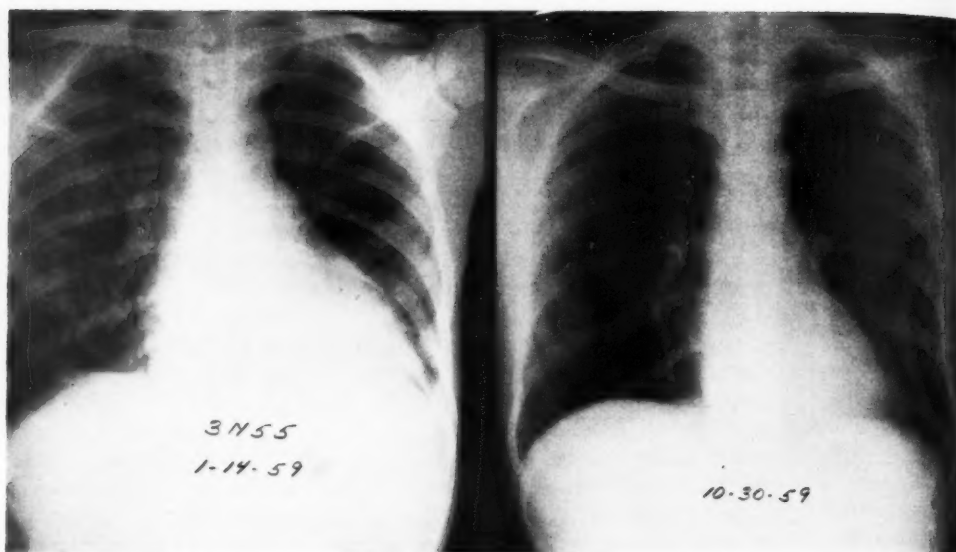


Fig. 4. Chest films of patient No. 3 (JR) prior to and ten months after total-body irradiation (450 r) and renal homograft from a fraternal twin.

ficity of the antibody-producing cells of the recipient, it was considered advisable to explore the use of the less penetrating 250-kv x-ray source, with fractionation of the total dose into two roughly equal amounts one week apart. The set-up employed is shown in Figure 5. Dose has been expressed as nominal air dose, uncorrected for back-scatter, to the midsagittal plane of the flank. Admittedly, this is an artificial exposure dose rather than an absorbed dose. However, because of inhomogeneity in the air-dose field at average treatment distances of 150 to 160 cm., and because of variations in distribution of body mass from one individual to another, it has not been felt that attempts to express the data as an average absorbed dose would lend particular precision or critical biologic meaning to comparative analyses. The orders of tissue dose magnitude measured in a Masonite phantom, with air space "lungs," of the same body proportions as patient No. 3 (JR), are shown in Table VII.

#### DISCUSSION

The use of total-body irradiation in the transplantation field has raised more ques-

TABLE VII: DOSIMETRY OF TOTAL-BODY IRRADIATION AT 250 KV

Body Site (Midsagittal Plane)	Rads/100 r*	Rads/450 r*
Flank	68	305
Mediastinum	82	370
Head	63	285
Maximum absorbed dose $\approx 30\%$ > minimum absorbed dose		

\* Nominal air dose midsagittal plane in flank

tions than it has answered. Nonetheless, there would appear to be a reasonable foundation for the belief that ionizing radiation will play a major role in progress in the homologous transfer of whole organs. In the dawn of this era, human experience will have been disappointing to those who want a complete and quick answer.

Temptation to demand that x-radiation do the complete job should not obscure the fact that its qualitative effects on the immune response due to histo-incompatibility mechanisms have all been in the right direction, despite great gaps in knowledge of procedural details.

The tendency has been to assume that homogeneity of total-body irradiation is important, but this is not known to be a fact. If it be decisive, methods of achiev-

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ing it in its most refined form have yet to be worked out fully. There is much that is not known about time-dose relationships, both with respect to gross fractionation and dose rate. Dose requirements as a function of the tissue to be transplanted and the timing of the homograft in relation to irradiation require further elucidation.

The basic question of whether tolerance to homologous organs in the human can be induced by "sublethal" irradiation must be left open. The prolongation of kidney-graft survival in patient JR suggests that, with respect to this organ at least, it can—if under circumstances of close consanguinity. Against the favorable background of the chronic uremic state (12), it remains to be seen whether, with greater genetic disparity between recipient and donor, there is a dose ascendancy which crowds the threshold of the difficult zone wherein the patient can do neither with nor without marrow. In the presence of a continuing stimulus from a large, vascularized antigenic mass, which is evidently granted some prolongation of survival even in the unirradiated recipient (13), one would hope that the recovery period from modest doses of depressant radiation might be characterized by an immunologic adaptation. The individual factors that apply to the transfer of whole organs other than the kidney are largely unknown.

Whichever the theory and whatever the dose range, the problems of guiding these already desperately ill patients through the post-irradiation course are many and varied. Scrupulous environmental hygiene and the administration of antibiotics, when needed, provide adequate control of exogenous infection, but the difficulties involved in combating infections that stem from the irradiated recipient's own bacterial flora are less easily solved.

As a final disquieting note, it must be recognized that the human counterpart of the graft-versus-host reaction in the laboratory animal presents an unknown but potentially foreboding cloud to overshadow the successful circumvention of the host-

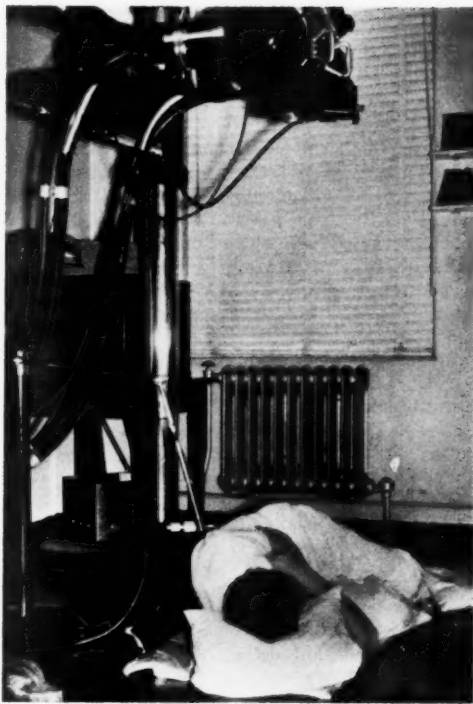


Fig. 5. Volunteer "patient" coiled up in 48-inch treatment oval for total-body irradiation from a 250-kvp constant-potential source. Target-floor distance is 176 cm.

versus-graft phase. The more optimistic side of the coin is that the virulence of this homograft reaction, if it occurs at all when the graft is a largely nonreactive organ in the immunologic sense, may be less in the heterogeneous human population than it is when one crosses highly inbred animal lines. The fact that the incidence of the reaction in severe form among our rabbit population has been less than might have been expected on the basis of work in mice and rats lends credence to this concept.

At the present time it would appear that continuing research must be directed:

- (a) Toward means whereby the impact of the acute radiation syndrome may be diminished without altering the biological effectiveness of radiation on the lymphopoietic and reticulo-endothelial systems.

- (b) Toward methods of enhancing the effectiveness of modest doses of irradiation on immunogenetic adaptive mechanisms.

NOTE: Both the animal and human studies reviewed briefly here represent the collaborative effort of a great many individuals on the staffs of the Peter Bent Brigham Hospital and Harvard Medical School. These include Drs. M. S. Brooke, P. Cohen, J. M. Corson, G. J. Dammin, E. A. Friedman, J. H. Harrison, F. Lee, J. P. Merrill, J. E. Murray, S. Piomelli, S. B. Rees, J. W. Retan, N. L. Sadowsky, C. W. Walter, and R. E. Wilson.

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Peter Bent Brigham Hospital  
721 Huntington Avenue  
Boston 15, Mass.

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*(Pro le summario in interlingua, vider le pagina 33)*



# Physical Considerations in the Design of Facilities for the Uniform Whole-Body Irradiation of Man

EDWARD W. WEBSTER, Ph.D.

WHOLE-BODY irradiation is currently being applied to man for several therapeutic purposes: the destruction of bone marrow as a preliminary to autologous (1), isologous (2), or homologous (3) bone-marrow grafting in the treatment of acute leukemia; the treatment of extensive radiosensitive malignant disease, such as lymphosarcoma, Hodgkin's disease, and seminoma (4), with or without subsequent autologous bone-marrow grafts; and suppression of the immune reaction, with or without subsequent homologous bone-marrow grafting (5), to permit homografting of other tissues.

It is generally considered that for these purposes a "uniform" whole-body dose should be delivered. This specification introduces two physical problems, namely the design of treatment facilities to administer a uniform whole-body irradiation dose and the evaluation of that dose. These problems are interlinked, since one must define the term radiation dose and consider the factors affecting its variation throughout the body before an arrangement for uniform whole-body dose can be specified.

## 1. THE SPECIFICATION OF DOSE

The words "uniform" and "dose" may each be interpreted in several ways. In whole-body irradiation procedures there has been no agreement on their meaning. Only rarely has "uniformity" in any sense been specified. Yet careful specification of these terms is necessary for reproducibility of scientific work or clinical treatment. Three varieties of "dose" are in use.

**"Air" Exposure Dose:** Doses in whole-body treatments, whether in man or animals, have usually been specified as the

exposure dose measured in roentgens in free air at some reference point. The two common points are the skin proximal to the radiation source and the midplane of the body. The variation of this air dose over the treatment zone may be cited. Such a simple specification has relatively little meaning by itself.

The exposure doses measured in roentgens at points on or in a body are, of course, considerably different from those measured in free air. In particular, both the quality of the radiation and the thickness and length of the body affect the "tissue" dose received from a given "air" dose.

**"Tissue" Exposure Dose:** It is more desirable to specify dose as the exposure dose measured in the body in roentgens. It is possible to specify the variation of exposure dose throughout the body, for example by citing an average dose and the per cent limits of variation. This dose has usually been calculated or measured for a solid phantom of unit density and for one axis or one plane in that phantom, depending on the geometry of the treatment method. Thus, specifications of exposure dose uniformity have ignored the irregularities produced by variations in the size of the body cross-section and by the presence of bone and lung.

**Absorbed Dose:** Dose may also be defined as "absorbed dose," a measure of the energy deposited per gram of tissue, for which the unit is the *rad*. If the treatment objective is to destroy all cells, or the vast majority of cells, of a particular type wherever they may be in the body, then it would seem desirable to deliver a minimum amount of energy to each of these cells. Similarly, if the objective is to inactivate a particular molecular

<sup>1</sup> From the Department of Radiology, Massachusetts General Hospital, Boston, Mass. Based on a paper presented as part of a Symposium on Bone Marrow Transplants and the General Immunological Problems, at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15-20, 1959.



species throughout the body, a macroscopically uniform energy deposition would seem desirable. In these events it would be preferable to specify dose and its variation in rads. In general, a given distribution of exposure dose in the body does not produce the same distribution of absorbed dose. The use of the latter measure introduces a complication in that it varies per roentgen, with the tissue type, and also for any given tissue depending on its proximity to other tissues. This variation is a function of radiation quality. Thus, a bone-marrow cell adjacent to the inorganic matrix of bone will receive more energy per roentgen of exposure than a cell which is further removed from the matrix (6-8), and this difference will change with radiation quality. To the extent that these nonuniformities in absorbed dose per roentgen have a significant biologic effect, their tedious evaluation in rads would be important. Fortunately, as will be discussed later (p. 23), it appears that these differences have little effect on the results of whole-body irradiation. Therefore, it would appear to be a needless complication in practice to elucidate those variations in absorbed dose dependent on tissue type. Moreover, the roentgen/rad ratio for soft tissue varies little over the range of x-ray qualities in general use for whole-body irradiation (see Table I) (9), so that the absorbed dose in soft tissue becomes the tissue exposure in roentgens multiplied by a constant.

Under the above circumstances, it appears immaterial whether dose in rads or "tissue" exposure dose in roentgens is specified. Factors which affect the biological response of the body must also be stated in order to complete the dose specification. Therefore, a description of the radiation quality and the time-dose relationship is also required.

## 2. LIMITATIONS OF UNIFORMITY

The degree of nonuniformity of (tissue) dose throughout the body which is tolerable for successful therapy of the types

TABLE I: ABSORBED DOSE IN RADS PER ROENTGEN OF EXPOSURE DOSE FOR TYPICAL PRIMARY X-RAY SPECTRA USED IN DEEP THERAPY

Peak kv	Filter (mm.)	h.v.l. (mm.)	Mean Conversion Factor	
			Water	Muscle
250	0.17Cu + 3 Al	1.0 Cu	0.95	0.95
250	0.9 Cu + 3 Al	2.0 Cu	0.96	0.96
280	...	3.1 Cu	0.97	0.965
400	...	4.0 Cu	0.97	0.97
1000	2.8 W 2.8 Cu	10 Cu	0.975	0.965
2000	3.1 Au	13 Cu	0.975	0.965
Cu <sup>60</sup>	...	...	0.974	0.965

\* From Handbook 62, National Bureau of Standards (9).

mentioned is unknown. Since one is presumably attempting to inactivate widely disseminated entities, acceptable uniformity might be said to reside between a minimum dose sufficient for inactivation and a maximum dose insufficient to produce lethal effects.

As an example, in the attempted treatment of leukemia with whole-body irradiation followed by the infusion of homologous bone marrow, the radiation dose delivered is that estimated to produce 100 per cent lethality as a result of bone marrow depletion, *i.e.*, the LD 100/30 dose. This dose level is very close to the limit of intestinal tolerance. Fishler *et al.* (10), for example, have observed that in one strain of rats for which the LD 100/30 was about 700 r, the delivery of 800 r produced death in five to six days from the acute intestinal syndrome, against which bone marrow offered no protection. Quastler has noted uniform deaths in rats in three or four days due to intestinal damage at doses of 1,000 r and over (11). The acute intestinal syndrome may also be induced by local irradiation of the whole abdomen. An upper limit of gross dose uniformity is therefore set by this consideration and may be regarded as an abdominal dose 15 to 20 per cent above the average. The lower limit, on the other hand, is set by the necessity to reduce the bone-marrow cell population to a sufficiently low and damaged level to prevent autogenous repopulation. This limit is not known. Jacobson, Marks

and Gaston (12) have observed, however, that marrow taken from isologous donors eight days after they have received 600 r of whole-body irradiation, is as effective as normal marrow in promoting survival in mice subjected to an LD 100 of 900 r. In a similar experiment, Berman and Kaplan (13) observed that equal numbers of nucleated marrow cells, whether unirradiated or irradiated with 400 r, conferred equal protection against LD 100 doses. Thus, the lower limit of uniformity may well be not more than 30 per cent below the average (LD 100) dose delivered. It would be expected, however, that this limit would depend on the type and volume of tissue receiving the lower amounts.

One might also derive the requirements of uniformity by considering the limits achieved in small animals in which successful homografts of bone marrow and other tissues have been made. In such experiments it is easy to arrange a relatively uniform distribution of exposure dose throughout the animal. For example, in mice irradiated unilaterally at 70 cm. F.S.D., with x-rays of 1.2 mm. Cu h.v.l., Corp (14) has measured a variation of exposure dose throughout the body of +8 per cent to -14 per cent about the dose in air at the midplane. This was the dose variation in mice which recovered from leukemia after LD 100 whole-body irradiation followed by bone-marrow grafting (15). With bilateral opposing fields in larger animals, a uniformity of  $\pm 5$  per cent can be obtained (14). The thickness of bone and lung is not great enough to modify this uniformity substantially. In man the tissue thicknesses in the radiation beam are much greater, rising to 35 cm. or more for radiation delivered laterally. This fact alone might lead to a non-uniformity of exposure dose of  $\pm 30$  per cent (16). The bones are thick enough, particularly in the pelvis, to produce radiation screening effects on tissue in their shadow. For example, as shown in Figure 1, 1 cm. of hard bone will reduce depth dose by 15 per cent with radiation of 1.5 mm. Cu h.v.l., and by 5 per

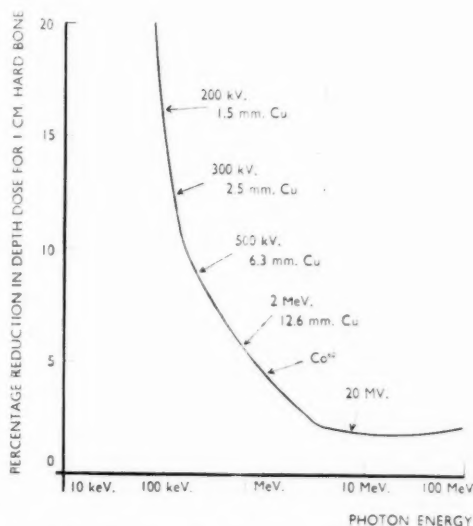


Fig. 1. Variation of shielding effect of 1 cm. of hard bone with photon energy. (From Meredith, W. J.: Some Aspects of Supervoltage Radiation Therapy. *Am. J. Roentgenol.* 79: 59, 1958. Reproduced by permission of the author and publisher.)

cent with  $\text{Co}^{60}$  gamma rays (17). On the other hand, the presence of lung increases the depth dose at other tissues in the beam path. For example, in a treatment with opposed fields normal to the coronal plane, with  $\text{Co}^{60}$  gamma rays, the anterior rib dose is calculated to exceed the sternum dose by 15 to 20 per cent. Thus, there are intrinsic limitations to dose uniformity in the human body of the order  $\pm 15$  per cent. In view of this unavoidable departure from the uniformity attainable in small animals, it is suggested that the nonuniformity which is design-dependent should be kept to a minimum. Somewhat arbitrarily, a ratio of maximum to minimum of 1.1 of exposure dose throughout a unit-density body is suggested.

### 3. KINDS OF UNIFORMITY

The expression of dose as exposure dose measured in the body, eliminates from our consideration the complex variations in absorbed dose in and near different types of tissue. Variations in exposure dose occur in three dimensions through the body; for convenience they may be

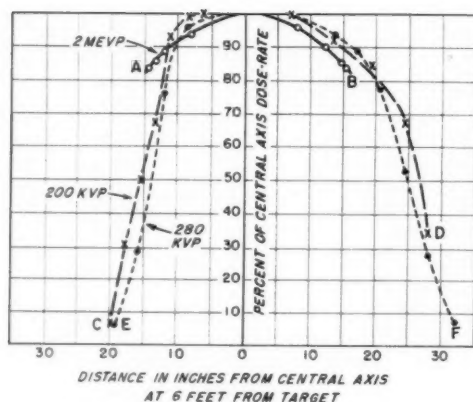


Fig. 2. Nonuniformity of exposure dose rates in free air across wide x-ray beams from machine generators. The maximum beam widths at 6 feet distance set by the primary collimation of the source housing are: AB 30 inches, CD 48 inches, EF 51 inches.

discussed in three geometric directions at right-angles to each other. Thus, there are variations in the anteroposterior direction and in the left-to-right direction in multiple planes distributed along the head-to-foot axis.

#### 4. TWO DESIGN PREMISES

Before discussing the design of whole-body irradiation facilities, it is necessary to distinguish between two premises on which designs may be based. Premise A is that the required spatial uniformity of dose throughout the body may be achieved by the *sequential* addition of two or more treatment fields. Under this premise the treatment may consist of two or more complementary irradiations, performed at different times, each producing a nonuniform dose distribution. Premise B is that the required uniformity must be obtained simultaneously in all tissues.

There appears to be little experimental evidence bearing on the necessity for simultaneity. The underlying idea is that a time-lag between nonuniform single irradiations may allow movement of some cells or other entities of importance so that they are always located in a zone of low dose-rate (3). In the case of leukemic cells in the general circulation, this is a cogent argument, which eliminates

divided field techniques. It is less certain that bilateral or multilateral fields, each covering the whole body but applied sequentially, would be less effective than simultaneous uniform treatment. In fact, in much experimental animal work in this area it is usual to employ sequential unidirectional fields. However, in the case of critically sick patients maintenance of one simple position throughout treatment would be preferable. Hence, simultaneity would be a desirable attribute of the optimal radiation facility.

#### 5. PREMISE A METHODS

##### *Single Radiation Source*

The simplest and most usual facility for the delivery of whole-body irradiation comprises one radiation source. The design of such a treatment would normally exclude the use of segmental partial body irradiations because of overlap or underlap uncertainties, which might well result in serious underexposure of some tissue volumes while producing an extensive overexposure in the abdomen which might prove lethal. Thus, it is desirable to plan a treatment with fields which encompass the whole body. The human body thickness is too large to permit treatment with one field only. Under certain circumstances adequate uniformity may be obtained with opposing bilateral fields.

*Choice of Distance:* The distance is determined by the requirement that the exposure dose rate over the area presented by the body must be uniform. If the body is prone or supine, uniformity must be achieved over a 6-foot transverse distance. For  $\pm 5$  per cent uniformity (max./min. = 1.1), the inverse-square law alone dictates a treatment distance of at least 9 feet. With machine sources of radiation, however, the polar variation of x-ray intensity with beam angle is more important than the inverse-square law. In Figure 2 the variation of dose rate across three wide x-ray fields is shown. For a typical 200-kv machine producing x-rays with a h.v.l. of 1 mm. Cu, a distance of 18 feet is required for an exposure dose



TABLE II: MAXIMUM AND MINIMUM DOSES RELATIVE TO 100 r MIDPLANE EXPOSURE DOSE IN AIR (20 X 20 cm. opposing fields; 110 cm. midplane distance; 20 cm. total thickness)

Radiation Energy (kev eff.)	80	108	135	165	198	240	369	560	801	1250	1500	2600
H.v.l. (mm. Cu)	1	2	3	4	5	6	8	10	12	(Co <sup>60</sup> )	(4 Mevp)	(8 Mevp)
Back-scatter Factor	1.46	1.40	1.35	1.30	1.25	1.21	1.15	1.11	1.075	1.05	1.04	1.02
Maximum Dose in r per 100 r (Air) at Mid-plane	106.7	103.8	100	95.6	91.6	89.5	86.5	87	85.9	85.3	86.5	90
Minimum Dose in r per 100 r (air) at Mid-plane	87.3	88.8	85.6	82.2	79.2	78.8	79.8	80.8	79.4	78.6	82.4	87.2

uniform to  $\pm 5$  per cent over a 6-foot span; and 13.5 feet for uniformity within  $\pm 10$  per cent. For a particular 2-Mev Van de Graaff generator,  $\pm 5$  per cent uniformity of air-exposure dose requires 22.5 feet, and  $\pm 10$  per cent uniformity 16.2 feet. These distances (even for  $\pm 10$  per cent uniformity) are greater than those normally available in rooms for conventional x-ray therapy.

To some extent the distance requirement may be minimized by the use of a "beam-flattening" filter which equalizes intensity across the beam. The treatment distance is then determined by the angle of the cone of radiation emerging from the primary collimation in the housing of the unit. For example, in the case (Fig. 2) of the Van de Graaff generator mentioned above, a beam of 6 feet width is subtended at a distance of 17 feet, while in the case of the 200-kv unit about 10 feet are required. Shorter distances may be utilized only with nonstandard housings. If a radioisotope source of gamma rays is used with a special wide-angle collimator and a beam-flattening filter to compensate for inverse-square law attenuation, a treatment distance of 5 feet would be feasible.

With these distances the radiation beam must be directed horizontally. It would be preferable to have the patient lie on each side in turn so that his anteroposterior thickness is presented to the beam. It may be desirable to treat very sick patients

in a supine position, but in that event dose uniformity through the body will suffer.

In an attempt to minimize the distance requirement, patients have been given whole-body irradiation in a sitting position with the head lowered onto the knees, opposed beams of radiation being delivered through the flanks. The patient may then be fitted into a circle of 36-inches diameter (18). Under these circumstances, the distances quoted above may be halved. Again, however, it is emphasized that the thickness of the patient presented to the beam will be the maximum lateral dimension.

When distances are as great as 3 meters, distance variation has little effect on the dose distribution through the body achieved with opposing fields. The depth doses are then essentially those obtainable with a parallel beam (infinite distance).

*Choice of Radiation Energy:* Since with conventional small fields, the quality of the radiation beam has a marked effect on depth dose, it is important to examine its effect on dose uniformity in whole-body treatment. In contrast to the wealth of information on depth dose distribution for small fields over a wide range of beam energy, little information is available for very wide fields. As a beginning, one may analyze central-axis depth-dose data for opposing 20 X 20-cm. fields in a phantom 20 cm. thick at 100 cm. F.S.D. for energies ranging from 200 kvp to 8 Mevp. The basic depth dose information is largely

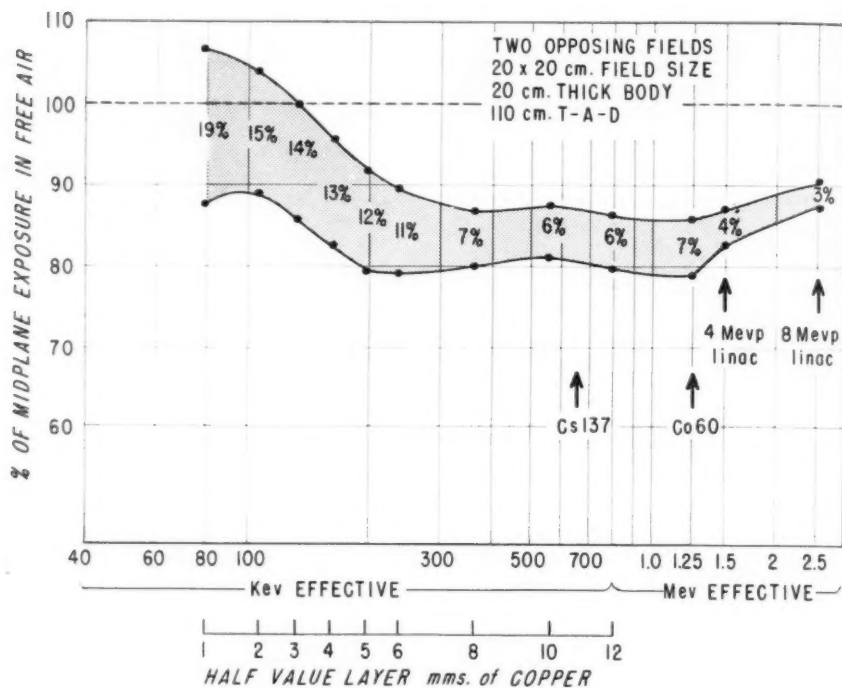


Fig. 3. Effect of beam quality on dose distribution through 20 cm. thick body with opposed wide fields.

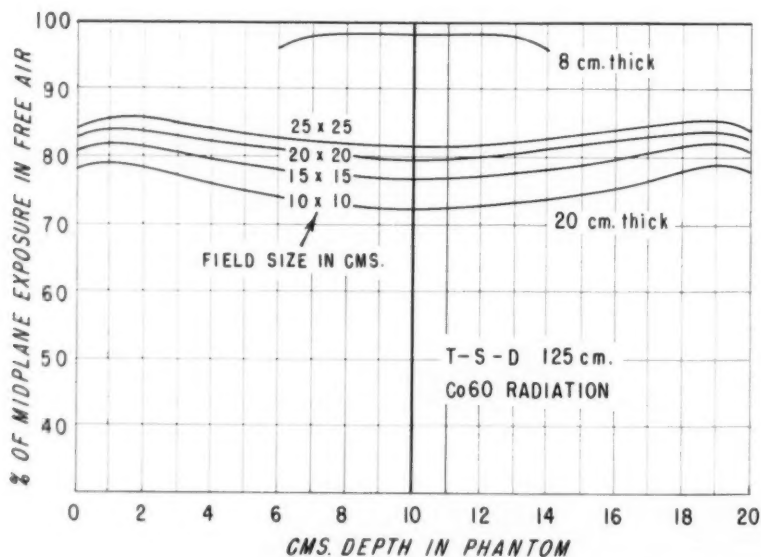


Fig. 4. Dose distribution with opposed fields and its variation with field size.

derived from Supplement 5 of the *British Journal of Radiology* (19). Back-scatter factors have been taken from a survey by Greening (20); for the higher qualities, average values of published data fitted to a smooth curve have been used (21). In Table II maximum and minimum doses throughout the phantom are presented as a percentage of air dose measured at the midplane. These figures are plotted in Figure 3. It is apparent that under these conditions the minimum and maximum doses remain at about 80 and 87 per cent respectively of the midplane exposure dose in air over a wide range of quality from about 7 mm. Cu h.v.l. to  $\text{Co}^{60}$  energies. At lower energies the divergence between maximum and minimum increases, but both are closer to the midplane air dose. At higher energies the divergence between maximum and minimum becomes smaller, and both approach 90 per cent of the midplane air dose; at these energies, however, there will be a zone of undertreatment at both skin surfaces.

Beside its usefulness in establishing values of exposure dose through an irradiated subject, the quotation of dose as a percentage of midplane air dose has another important significance. For high radiation qualities the dose delivered to relatively thin regions of the body, such as the lower limbs and the neck, will closely approach this midplane air dose (Fig. 4). Hence, the divergence between the minimum dose and the air dose (100 per cent) is a measure of the nonuniformity of treatment along the axis of the body.

It is to be expected that increases in field size beyond  $20 \times 20$  cm. will produce a small improvement in the ratio of maximum to minimum and cause them to be more nearly equal to the midplane air dose. Figure 4 is plotted from the  $\text{Co}^{60}$  depth data of Dixon, Garrett and Morrison (22) at 125 cm. source-skin distance, which includes a field size of  $25 \times 25$  cm. At this field size the maximum dose is only 4.7 per cent greater than the minimum; 1.7 per cent is attributable to the inverse-square law. Hence, at distances of

TABLE III: EFFECT OF TISSUE THICKNESS ON DOSE UNIFORMITY FOR BILATERAL TREATMENT

Tissue thickness (cm.)	Per cent of Midplane Air Dose					
	h.v.l. 3 mm. Cu			Cobalt 60		
	Midplane	Max.	Max/Min.	Midplane	Max.	Max/Min.
10	126	126	...	96.1	96.1	...
14	114	114	...	89.8	90.7	...
18	100.7	102.6	1.018	84	86.5	1.03
20	94.9	99	1.06	80.5	84.6	1.05
24	83	94.5	1.14	74.6	81.3	1.09
28	70.7	90.3	1.28	68.8	79.5	1.16
32	60.8	88	1.45	62.5	78.4	1.25
35	55.1	87.5	1.59	58.4	78	1.34

From Sinclair and Cole: 3 mm. Cu, 1200 sq. cm., 190 cm. F.S.D. (16). Dixon, Garrett, and Morrison: Cobalt 60, 625 sq. cm., 125 cm. F.S.D. (22)

several meters, a difference between maximum and minimum of only 3 per cent is expected through a section 20 cm. thick.

It is evident that with supervoltage radiation a more uniform dose will be delivered to a volume of tissue with a constant thickness of 20 cm. than with 200 to 400-kvp radiation. Table III extends this finding and shows that greater uniformity is also achieved by supervoltage radiation in the treatment of bodies of variable thickness. This table has been calculated from the depth dose data of Sinclair and Cole (16) for x-rays of h.v.l. 3 mm. Cu, with fields of 1,200 sq. cm., and of Dixon, Garrett, and Morrison (22) for  $\text{Co}^{60}$  gamma rays with a field size of 625 sq. cm. It is apparent that, with the lower quality of radiation in a body of 20 cm. maximum thickness, the dose varies from 95 to 126 per cent of the midplane air dose, whereas with  $\text{Co}^{60}$  the variation is from 80 to 96 per cent. If, however, the radiation is delivered through the flanks of a patient with a lateral hip dimension 35 cm., the situation is much worse; the variation at 3 mm. Cu h.v.l. being from 55 to 126 per cent of the midplane air dose, and with  $\text{Co}^{60}$  58 to 96 per cent.

Bond *et al.* (23) have measured the dose distribution in a cylindrical phantom 26 cm. long and 26 cm. in diameter, irradiated with  $\text{Co}^{60}$  gamma rays at a source-skin distance of 100 cm. The doses at the skin and at the cylinder axis were 79 and 70

per cent respectively of the axis air dose. These figures agree well with those in Table III.

In order to determine whether better uniformity than that suggested above for  $\text{Co}^{60}$  would be secured for whole-body irradiation, preliminary measurements have been made in an elliptical Masonite phantom. The dimensions were those of the lower trunk of an average adult (20 cm. anteroposterior  $\times$  35 cm. lateral  $\times$  25 cm. high). The phantom was irradiated with 2-Mev x-rays and with radium gamma rays. Relative exposure dose measurements were made with air wall ionization chambers 1 cm. in diameter, at points along the central axis. The results, summarized in Table IV, confirm

TABLE IV: MEASUREMENTS OF UNIFORMITY FOR WHOLE BODY BILATERAL IRRADIATION

Radiation	h.v.l. (mm.)	Source to Mid- plane (cm.)	Ratio Max./Min. Dose	
			A-P fields	Lat. fields
2 Mevp X Radium	13 Cu ...	125	1.04	1.35
		122	1.035	...

the calculations of Table III for 20 cm. and 35 cm. tissue thicknesses and  $\text{Co}^{60}$  gamma rays.

It is therefore not possible to irradiate an adult human body with opposed radiation fields through the flanks and achieve a dose distribution uniform to  $\pm 5$  per cent. Even with  $\text{Co}^{60}$  gamma rays, the uniformity through an unbolussed adult body would be about  $\pm 25$  per cent. With opposed anterior and posterior fields, it is possible with  $\text{Co}^{60}$  or similar hard radiation to attain about  $\pm 10$  per cent uniformity without bolus. If the body is bolussed to a uniform thickness, then a uniformity of dose better than  $\pm 5$  per cent can be achieved. These calculations ignore the inherent nonuniformity produced by bone and lung.

It has been suggested (3) that the non-uniformity of absorbed dose in the marrow is a further reason for the use of super-voltage radiation in whole-body treat-

ments. Spiers (6) and Wilson (7) have discussed the nonuniformity of ionization that occurs in soft tissue close to hard bone, due to the greater electron flux generated in the bone by x-rays. Thus x-rays of 1.5 mm. Cu h.v.l. will produce about twice as much ionization per cubic micron in marrow cells adjacent to bone cortex as in cells farther from the cortex than the electron equilibrium distance. On the other hand, for 2-Mevp x-rays the difference is only a few per cent. Bone marrow will therefore absorb more energy per roentgen at low radiation energies than at high radiation energies. Recently, however, Epp, Woodard, and Weiss (8) have calculated in detail the average absorbed dose received by the bone marrow of mice per roentgen of 250-kvp x-rays and of  $\text{Co}^{60}$  gamma rays. They conclude that the difference in average dose is not more than 5 per cent. Moreover, Sinclair, Blackwell, and Humphrey (24) have measured the relative biological effectiveness of 200-kvp x-rays and  $\text{Co}^{60}$  gamma rays in producing bone marrow damage as indicated by changes in iron uptake. Sinclair has concluded (25) that this relative biological effectiveness is little different from that with other biological end-points not involving bone marrow. Hence, the nonuniformity of ionization in bone marrow does not appear to be a significant factor in producing lethality and is not, therefore, a cogent reason for using high-energy radiation.

Meredith (17) has calculated the extent to which a layer of bone will shield tissue beyond it in a beam of radiation. The per cent change in depth dose per centimeter of hard bone is given in Figure 1 as a function of radiation energy. In the adult human pelvis it is estimated that thicknesses of cortical bone up to 2 cm. may be encountered by radiation traveling inward toward the body axis. The depth doses in the shadow of a 2 cm. thickness will be reduced by 30 per cent with x-rays of 2 mm. Cu h.v.l. and by about 10 per cent with 2-Mevp or  $\text{Co}^{60}$  radiation. Some of the marrow inside these bones

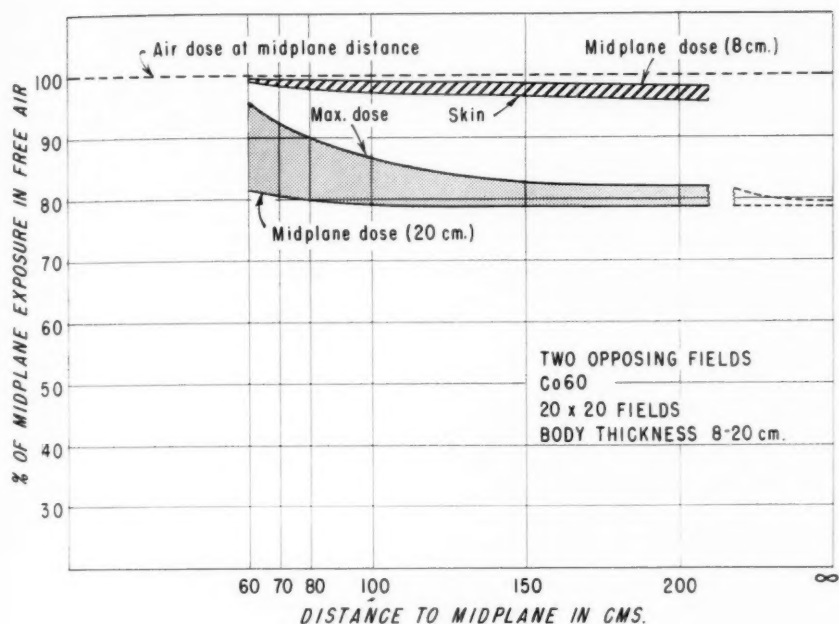


Fig. 5. Effect of treatment distance on dose uniformity.

will be shielded by approximately these same amounts. The relative lack of shielding by bone constitutes a further good reason for using high-quality radiation—in this case, the higher the better.

In summary, the principal disadvantage of conventional single sources is the large treatment distance necessary for acceptable dose uniformity, and hence the large treatment room which would normally require special design. The radiation source-strength for a given treatment dose rate likewise becomes great, since it is utilized very inefficiently. A further disadvantage is the undesirability of treating a sick patient lying on his side for long periods of time, which is necessary if reasonable uniformity is to be attained in adults.

#### Multiple Sources

Uniformity of dose equal to that attainable with a single source may be achieved in a smaller room and with smaller source strengths by employment of more than one source. Moreover, the patient may then be treated in the prone and supine positions,

while securing the best available uniformity of dose.

With two sources arranged in the central sagittal plane, the treatment distance for achieving air dose rates uniform within  $\pm 5$  per cent is only 3 feet to the midplane of the patient. With three sources arranged along a line in the central sagittal plane the treatment distance may be even shorter.

Reduction of the distance of the radiation sources from the body causes two effects which must be examined before an optimum distance may be chosen.

*Choice of Distance:* The distribution of exposure dose through a body 20 cm. thick, irradiated bilaterally, is essentially uniform at treatment distances greater than 1 meter. The distribution becomes less uniform at shorter distances because of the inverse-square law. This is illustrated in Figure 5, prepared from standard depth dose tables (19) for  $\text{Co}^{60}$ , with the largest quoted field size,  $20 \times 20$  cm. At 60 cm. to the midplane, the midplane dose is 85 per cent of the maximum dose. The figure shows, however, that the overall



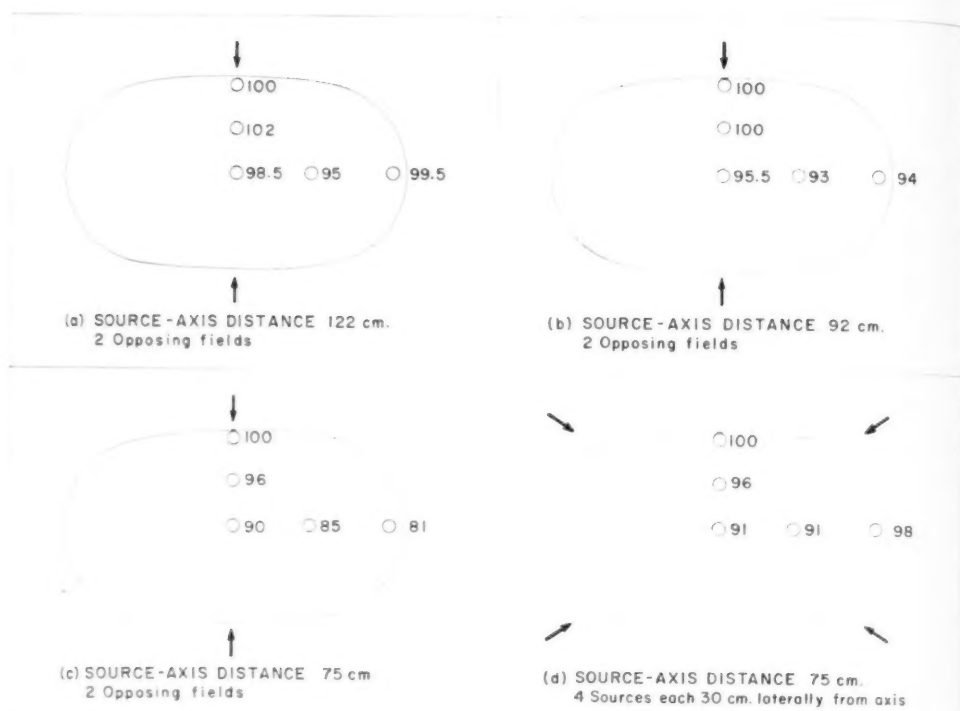


Fig. 6. Dose distributions through body section from wide opposed fields of radium gamma rays: effect of source-axis distance and source distribution.

variation between dose to the thick sections of the body (e.g., abdomen) and to the thin sections (e.g., neck or legs) does not change much with treatment distance. We conclude that the degree of uniformity over the whole of an *unbolussed* body is not significantly affected by the source to midplane distance down to 60 cm.

A series of experiments has been performed to examine the effect of source distance and source arrangement on the dose distribution throughout a solid Masonite phantom of elliptical shape, as previously described. Comparative measurements of exposure dose were made at five strategic points in one plane in the middle of the phantom, which was irradiated bilaterally from anterior and posterior aspects with two or more radium sources. The results are shown in Figure 6. As the source-axis distance is reduced from 122 to 75 cm., the ratio of maximum to minimum dose in the central sagittal

plane falls, as previously predicted. More important, however, is the reduction of dose at the flanks of the phantom when the source distance falls below 3 feet (92 cm.). This is presumably due to increased oblique tissue absorption as the distance is reduced. The limitation can be overcome by doubling the number of sources and moving their position to paraxial planes located laterally to the phantom. Figure 6 (d) shows measurements made with four radium sources located symmetrically on opposite sides of the phantom, the sources on each side being 60 cm. apart. This distribution should be compared with Figure 6 (c).

With three or more sources arranged collinearly on one side of the patient, it is necessary that the end sources be stronger than the central source or sources in order to obtain axial uniformity of dose. Thus, with three sources at 3 feet from the body axis, each end source should have a

strength 250 per cent of that of the central source. The axis air dose is then uniform to within 2 per cent.

*Special Multiple-Source Designs:* Two limiting examples of multiple-source arrangements designed for opposing field treatments are an extended line source and an extended area source. Unless these sources are considerably more extensive than the body to be treated, they must be nonuniformly loaded. Thus, a line source would be of the "dumb-bell" type described by Tooze (26) for radium therapy, with increased source concentration at the ends of the line. The area source would require some peripheralization of the source material along the lines of the Paterson and Parker rules for radium surface applicators.

Hummon and Landauer (27) have constructed a linear source 200 cm. long, containing cesium 137. Their measurements show that at 60 or 80 cm. from the source, the dose rate is tolerably uniform over about 60 per cent of the length. Hence, for a 6-foot long man, the source length required would be about 3 meters or 10 feet.

Whole-body irradiation units of this type could be installed in the vicinity of nuclear reactors where the radiation source could be a radioactive gas or liquid, preferably of short half life, circulated through the reactor and through containing tubes external to the reactor. Such loops, using liquid metals such as an indium-gallium eutectic with high thermal neutron cross-sections and gamma-emitting products of short half-life, are presently under development (28) for the industrial irradiation of pharmaceuticals and plastics. A thermal reactor itself with modifications of the shielding would provide an extensive area source of desirably energetic gamma rays, producing a uniform radiation field over the 6 X 2.5-foot area of the supine, prone, or standing patient.

#### 6. PREMISE B METHODS

If premise B is accepted, then it is not possible to move the patient or the

radiation source for sequential treatments. It then becomes necessary to provide a composite radiation field, producing a uniform dose rate throughout the whole body. This may be done by providing mirror images of the systems discussed above. This would nearly double the cost of the irradiator and may double the size of the treatment room required.

*Two-Source Unit:* Unless beam-flattening filters are employed, teletherapy units containing gamma-emitting sources of cylindrical profile (to equalize self-absorption), should be 18 feet apart for  $\pm 5$  per cent uniformity of air exposure dose. With beam flatteners and special wide-angle collimators, the distance could be reduced to 10 feet. Machine sources would require much more severe beam flattening for use at this latter distance.

*Four-Source Design:* If four sources are located at the corners of the mid-sagittal plane with two above the body and two below the body, 6 feet apart, then the optimal distance above and below the central plane yielding air dose uniformity to  $\pm 1$  per cent is 4.25 feet. If the sources are brought in to 3.5 feet from the central plane, the air dose uniformity drops to  $\pm 5$  per cent. An improvement at this distance is effected if the distance between the sources is changed to 5 feet, which produces an air dose uniformity of  $\pm 2$  per cent over a 6-foot distance along the principal axis.

*Six-Source Design:* The major reason why a six-source unit might be preferable to a four-source unit is the shorter source distance, which allows smaller source strengths to be used. It has already been shown, however, that 3 feet is the minimum distance from centrally placed sources to give adequate dose to the flanks. Hence, this design will have little or no advantage over the simpler, more economic four-source unit.

*Eight-Source Design:* As mentioned above, the substitution of two laterally-placed sources for each central source will increase the dose delivered to the flanks of a supine patient. This is of

importance only for source distances less than 3 feet. In general, it would be more economical to use as few sources as possible (especially if in teletherapy housings) at the cost of longer source distance and greater source strength.

**Cylindrical Sources:** The simultaneous bilateral systems of point sources, line sources, or parallel planes may be elaborated into multilateral systems of which

expectation that a cylindrical source produces a distribution almost identical with that obtained with bilateral irradiation. In fact, similar diametral distributions are obtained for a ring source, a 4 $\pi$  (spherical) source, multilateral, and bilateral exposures. The human body, however, has an elliptic section. This causes regions of high dose to occur at the flanks of a patient when treated with a

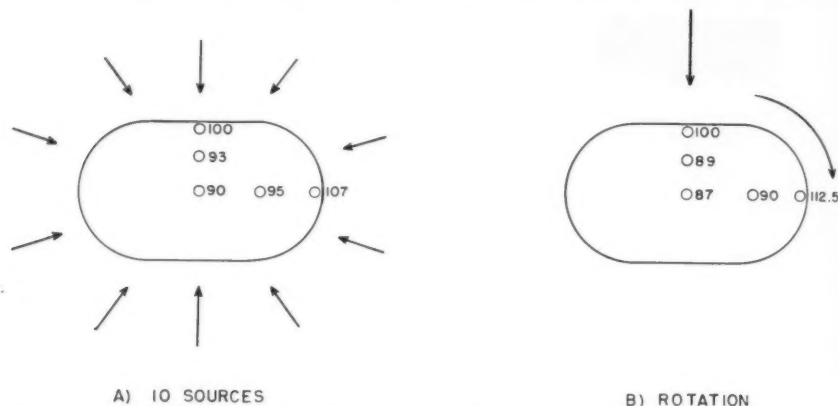


Fig. 7. Dose distribution in elliptical body from radiation field with cylindrical symmetry.  
A. Circle with ten radium sources, 3-foot radius.  
B. Rotation with 2-Mevp x-rays, target-axis 3 feet.

the practical end-point is a cylindrical irradiator encompassing and coaxial with the body. Spiers has discussed in great detail the distribution of exposure dose in free air inside cylinders of a wide range of geometry, uniformly loaded over their cylindrical surface (29). The dose pattern has cylindrical symmetry, with dose falling from the central plane toward the ends of the cylinder and rising radially toward the wall of the cylinder. For example, inside a cylinder 3 feet in diameter and 6 feet long, the central axis air dose varies from 100 to about 60 per cent and from 100 to 110 per cent over the central 18-inch diameter cylinder. For whole body irradiation this axial variation must be corrected, as for the line source, by heavier loading of the cylinder ends.

The work of Bond *et al.* (23), who have measured the dose distribution in a *cylindrical* phantom 26 cm. in diameter, irradiated with Co<sup>60</sup> gamma rays, confirms the

cylindrical source or with a wide rotating beam. The effect is due to the inverse-square law and to the increased tissue absorption across the lateral dimension. In a 20 × 35-cm. body section, the dose distribution with a cylindrical or rotational approach is notably poorer than that achieved with opposed anterior and posterior fields. Figure 7 illustrates this conclusion. The 20 × 35-cm. elliptical phantom previously described was irradiated by a ring source consisting of ten equal radium sources spaced evenly around a circle of 3 feet diameter. Figure 7, A shows the relative dose rates measured at 5 strategic points. With wide-field 2-Mevp x-ray data, the distribution was calculated for the same five points for a rotational "whole-body" treatment with a target-axis distance of 3 feet. This result, shown in Figure 7, B, agrees fairly well with the experimental result, and emphasizes the lateral nonuniformity.



## 7. EXISTING WHOLE-BODY IRRADIATION UNITS

There are presently at least three specially designed installations for whole-body irradiation in the United States. These illustrate the advantages and disadvantages of several approaches we have discussed.

The earliest installation was at the Naval Medical Research Institute (30) in Bethesda, Maryland. It consists of 100 separate  $\text{Co}^{60}$  slugs which are transferred pneumatically in 60 tubes from a storage place into predetermined positions on a surface surrounding an animal or patient. This unit attempts to provide a spherical source surrounding the body and has the same limitation of dose non-uniformity as would a cylindrical source. The presence of such a large number of moving sources has produced maintenance problems mostly concerned with source leakage and the effects of radiation on the washers which support the radiation sources as they slide in the manifold tubes. From a maintenance and cost point of view, a few single sources would be better.

Drs. Sahler, Ferree, and Thomas (3, 31) at the Mary Imogene Bassett Hospital in Cooperstown, New York, have two  $\text{Co}^{60}$  teletherapy units arranged to irradiate a patient bilaterally in wide, horizontal beams. If an adult patient is prone or supine, there will be dose uniformity of the order  $\pm 30$  per cent, as discussed earlier. The treatment room has been specially designed so that it allows a distance of 3 meters from each source to the axis of the patient and has an overall length of 23 feet. The concrete walls have a thickness greater than 3 feet.

A third, specially built facility has been designed by Mr. Leon Pape at the City of Hope Medical Center in Duarte, California (32, 33). This unit follows the principles of the eight-source design discussed earlier and provides the most uniform dose distribution of these three units. The sources are each 300 curies of cesium  $^{137}$  and are arranged in two planes, each

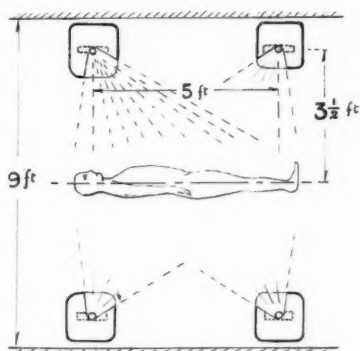


Fig. 8. Four-source total-body irradiator. Uniformity of exposure dose in free air at midplane  $\pm 2$  per cent. Overall uniformity of exposure dose in unbolussed body 20 cm. thick  $\pm 10$  per cent.

containing four sources at the corners of a cuboid 6 feet high, 6 feet long, and 5 feet wide, with the patient along the central longitudinal axis.

## 8. OPTIMUM FACILITY DESIGN

There are clearly many methods by which acceptable dose uniformity may be achieved. The merit of different facilities may, however, be judged on the basis of the following desirable characteristics:

1. Small size, to minimize the capacity and cost of the radiation source, the necessary shielding, and the necessary allocation of building space.
2. Source disposition above (and possibly also below) a patient to allow anterior and posterior treatment in the supine position.
3. A minimum number of sources to reduce costs of housings, maintenance, and renewal, and to reduce hazards of leakage, contamination, or jamming with radioisotope sources.
4. A simple procedure for source exposure and cut-off.

A four-source design utilizing  $\text{Cs}^{137}$  is shown schematically in Figure 8. It appears to satisfy most of these criteria. The source distance is large enough to give adequate dose uniformity while allowing the whole unit to fit into a therapy room of conventional size and height. The well developed technology of teletherapy hous-

ings is utilized, although the collimation requirements are unusual. Primary beam protection is limited to the regions above and below the unit.

The use of units such as this, which provide a high degree of dose uniformity, permits the accurate translation to the patient of techniques developed with small experimental animals. It may well be that the clinical usefulness of whole-body irradiation can be demonstrated only in these costly and special facilities.

Massachusetts General Hospital  
Boston 14, Mass.

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## SUMMARIO IN INTERLINGUA

**Considerationes Physic in le Planning del Dispositivos pro le Uniforme Irradiation del Corpore Total de Patientes Human**

In nostre dies le applicationes therapeutic de irradiation del corpore total include (1) le destruction del medulla ossee como mesura preliminar al graffage de medulla ossee in le tractamento de leucemia acute, (2) le tractamento de extense morbos maligne de typos radiosensibile, e (3) le suppression del reaction immun pro render possibile le homograffage de tissu.

Pro iste objectivos un uniforme dose al corpore total es desirabile. On pote dicer que un grado acceptabile de uniformitate es attingite si le dose remane inter le minimo sufficiente a inactivar le cellulas que debe esser destruite e un maximo non sufficiente a producer effectos letal.

Il existe multe methodos que permette le effectuation de un acceptabile grado de uniformitate del dosage. Le meritos de iste methodos pote esser judicate super le base del sequente criterios:

1. Micre dimensiones, a fin de reducer le capacitate e le costo del fonte de radiation, del requirite armatura, e del provision de spatio.

2. Disposition del fontes supra (e possibile etiam infra) le patiente pro permitir le tractamento anterior (e posterior) con le patiente in decubito dorsal.

3. Le plus basse numero possibile de fontes, a fin de reducer le costo del conchas, del mantenentia, e del reimplaciamento e a fin de eliminar in tanto que possibile le riscos de escappamento, de contamination, o de interferentia quando radio-isotopos es usate como fontes.

4. Simplicitate technic del manipulation pro iniciar le exposition e pro obturar lo.

Un arrangiamento a quatro fontes, con le utilisation de cesium-137, pare satisfacer le majoritate de iste criterios.

## SUMMARIO IN INTERLINGUA

**Le Theoria e le Practica del Irradiation de Corpore Total in le Era del Advenimento de Homograffage**

(Pagina 11)

Le function del irradiation del corpore total como preparation al transplantamento de tissu inter geneticamente non relationate subjectos jace in le effectuation de alterationes in le responsas de anticorpore. Il existe duo conceptiones theoric con respecto al effectuation de iste phenomenos immunologic. Un de illos demanda alte doses de irradiation (de un ordine de magnitude que es potencialmente letal), e le altere labora con basse doses. Le prime del duo pare esser superior. In conilios, le melior protection per homologue medulla ossee contra 250 kv de irradiation del corpore total esseva obtenite post un dose total de 1.100 r administrate in duo portiones con un die de intervallo.

Post potencialmente letal doses de radiation, infusiones de medulla ossee resulta in un reimplaciamento functional del me-

dulla del recipiente, e on pote expectar que illos provide un efficace supporto durante le phase acute del syndrome de radiation. Successose graffos de medulla, representante un nove systema de recognition immunologic, deberea esser tolerante con respecto a altere graffos de tissu ab le mesme donator o ab un donator de identitate genetic. Il ha essite constatate que animales que accepta tal infusiones es etiam preste a acceptar transplantationes de pelle ab le donator del medulla.

Essayos de applicar le resultatos experimental al practica clinic esseva interprendite in le casos de 6 patientes. Un esseva un masculo de 23 annos de etate in qui un ren esseva transplantate ab un gemino dizygotic. Le patiente esseva vive e clinicamente ben dece menses post le operation.

# Coronary Arteriography: Development of a Method in Animals with Particular Attention to Physiologic Effects<sup>1</sup>

SIDNEY W. NELSON, M.D., WILLIAM MOLNAR, M.D., ANTHIMOS CHRISTOFORIDIS, M.D.,  
and CLARENCE BRITT, M.D.

**N**EW SURGICAL approaches (1, 2, 9) offer some hope to the many persons suffering from occlusive disease of the coronary arteries. The rational selection of patients for surgery and, indeed, the outcome of the operation itself will certainly benefit by a reliable, precise method of preoperative localization of diseased segments of these vessels and the clarification of the state of the collateral circulation, if such exists. Many investigators (3, 4, 5, 9, 12, 13, 15) have reported methods of radiographically visualizing the coronary circulation in living animals, and others (7, 8, 10, 15, 17, 18) have used varying technics in man. Recognizing the need for a practical clinical method of portraying the coronary artery circulation, our group decided to approach this goal by modifying our previously reported method of aortic valvulography (14), inasmuch as this technic was already an accepted and useful tool in our institution. It is the purpose of this paper to describe the method of coronary arteriography worked out in the animal laboratory, with special emphasis upon the physiologic effects.

## METHOD OF STUDY

In our animal studies 350 injections were performed in 50 mongrel dogs. No attempt was made to appraise contrast materials, our efforts being directed toward evaluating the opacification of the coronary arteries as we varied catheters, speed of injection, injection pressure, amount and concentration of contrast medium, phase of the cardiac cycle during which the injection was initiated, etc. During the evaluation of these variables, we were

also interested in the electrocardiographic changes occurring during and after all injections.

The right common carotid artery was used as the point of entry for the catheter, which was then passed through the brachiocephalic trunk into the ascending aorta. Early in our experiments the tip of the catheter was placed in the desired supra-valvular region under fluoroscopic control. After some experience, it was learned that the location of the catheter tip could be accurately estimated by virtue of the appearance of a rather vigorous to-and-fro movement—2 to 3 mm.—of the entire catheter as it approached the valve region. If the catheter was inadvertently passed into the descending aorta, this movement was minimal and did *not* increase in amplitude. A very noticeable increase in amplitude as the catheter was gently advanced through the incision in the right carotid artery was proof that the tip was approaching the aortic valve.

## TYPES OF CATHETER

Our previous investigations (14) had shown that the use of a single-side-opening, closed-end catheter precluded the loss of contrast material through the normal aortic valve into the left ventricle. With the transcarotid approach, however, the tip of the catheter usually became located near the left coronary artery ostium because of the normal anatomic factors in dogs. With this location, visualization of the right coronary artery was often poor if a catheter with a single side-opening was used, though extremely good demonstration of the left coronary artery was obtained. In order to attain good simulta-

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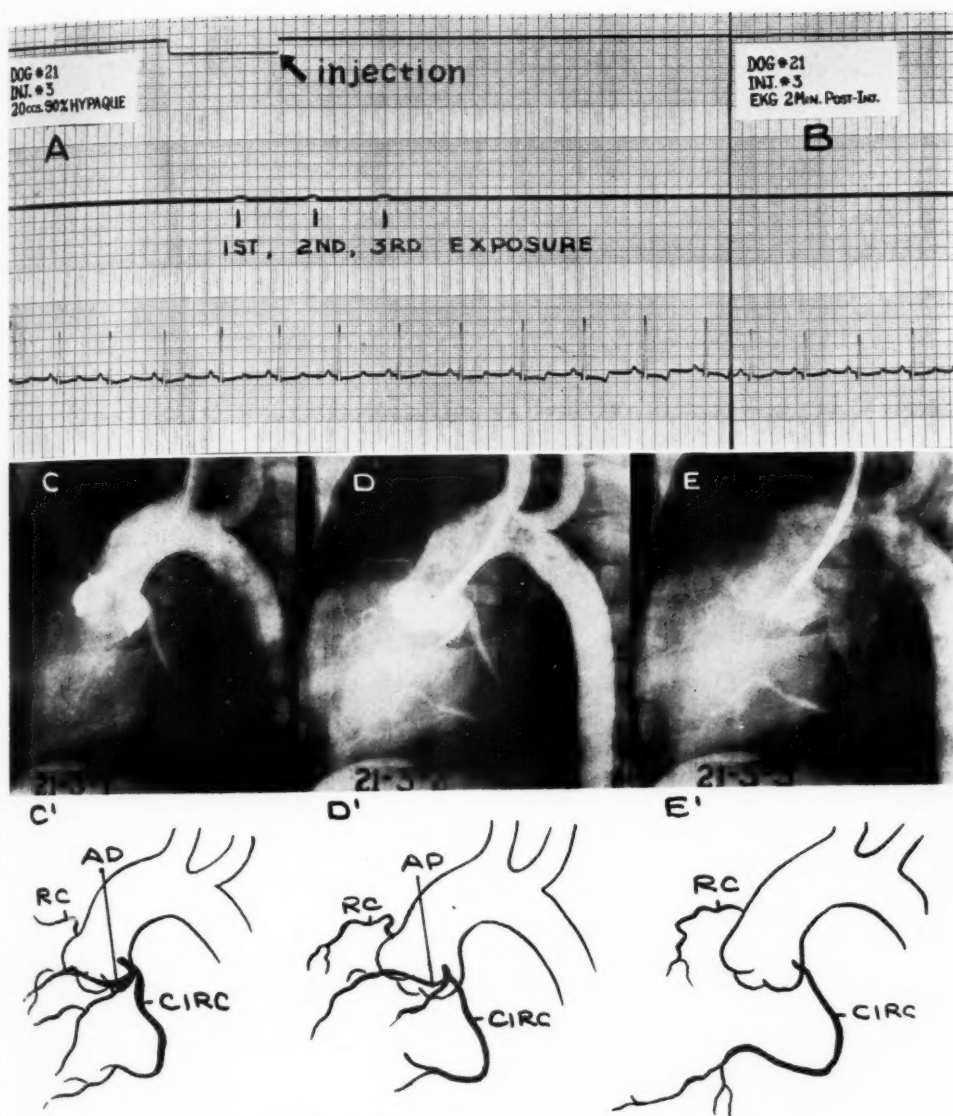


Fig. 1. A. Routine method for correlating injections and exposures. The top signal records the duration of the injection which is triggered by the R wave following the closing of the relay circuit. The injection begins almost simultaneously with the end of the R wave. The second signal indicates the exposures. The first exposure can be made at any time desired after the injection begins by setting the second relay. Thus it is possible to make this first exposure during any phase of the cardiac cycle.

B. Post-injection electrocardiogram for study of reversibility of electrocardiographic changes. C, D, and E are the three consecutive exposures made in lateral position in a total elapsed time of 1.2 seconds, as recorded in A. Time of exposures can be exactly correlated with the cardiac cycle and with the injection by studying the recording of these data in A. The first exposure (C) was made during late systole, as can be seen on the recording, which shows that this exposure was made late during the ST-T part of the cardiac cycle. This correlated well with the appearance on the exposure, which shows the aortic valve open. The second exposure (D) was made during early diastole, between the end of the T-wave and the subsequent P-wave. This correlates well with the appearance on the exposure, on which the aortic valve is seen to be closed. The third exposure (E) was also made during diastole of the subsequent cardiac cycle.

C', D', and E' are line drawings of C, D, and E respectively. The right coronary artery (RC), anterior descending (AD), and circumflex (circ) branches of the left coronary artery are indicated.



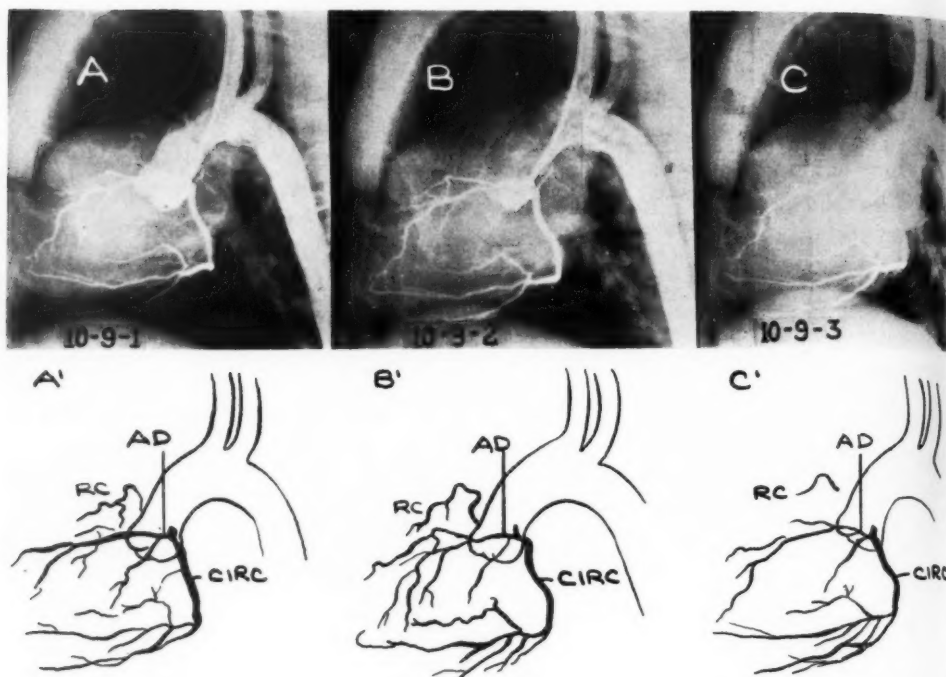


Fig. 2. Three consecutive exposures made during a total elapsed time of 1.2 seconds. First exposure (A), made near the completion of a one-second injection of 20 c.c. of 90 per cent Hypaque, shows good visualization of the major coronary arterial branches.

Second exposure (B), made 0.6 second later, still demonstrates good visualization of the major coronary arteries. The proximal aorta is now being cleared of the contrast material by the nonopaque blood ejected from the left ventricle.

Third exposure (C), made 1.2 seconds after the first exposure, reveals almost complete clearing of the aorta. The contrast is now diminishing in the proximal branches of the major coronary arteries.

A', B', and C' are line drawings of A, B, and C respectively, showing right coronary artery (RC), anterior descending (AD), and circumflex (CIRC) branches of the left coronary artery.

neous visualization of both coronary arteries, we decided to try multiple-side-opening catheters made of nylon tubing in lengths varying from 14 to 16 inches, with an inside diameter of 2.5 mm. and an outside diameter of 3.5 mm. The ends are closed and six to eight small side openings are easily drilled through the wall of the distal 10 to 15 mm. A No. 13 intravenous needle can be inserted into the proximal open end of such a catheter, and will fit so tightly that there is no leakage of contrast material during rapid injection under high pressure. The catheters are cheap and can be discarded, except for the needle, after each use. They were easily introduced through the carotid artery and allowed rapid injection of concentrated

contrast material into the entire aortic valvular region, with subsequent improvement in the simultaneous visualization of the left and right coronary arteries (Figs. 1 and 2).

#### LOCATION OF TIP OF CATHETER

It was found necessary to inject the contrast material as near as possible to the coronary ostia. It was therefore essential to position the tip of the catheter close to the aortic valve. The previously mentioned characteristic to-and-fro movement of the catheter became vigorous when the catheter tip approached a point 1 to 2 cm. above the valve. This method of placing the catheter tip gave consistently excellent results without need for fluoros-

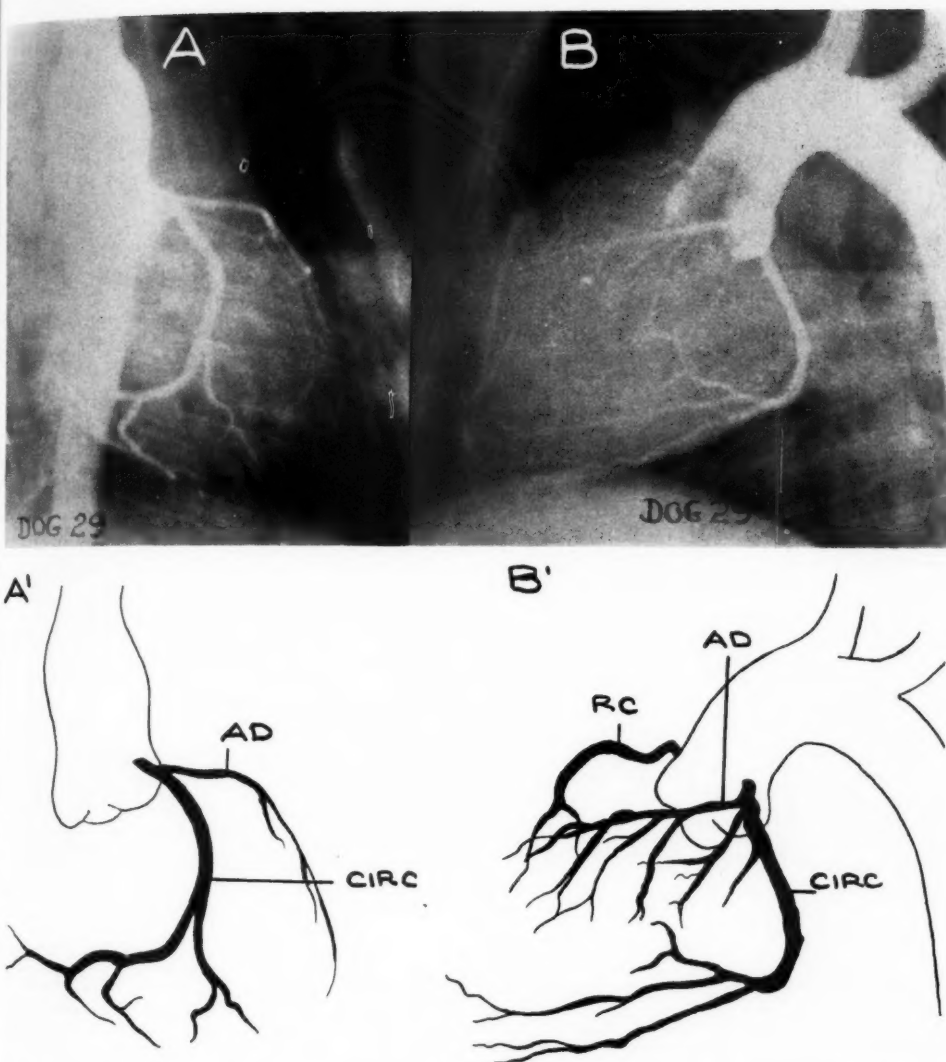


Fig. 3. Simultaneous biplane exposures with the animal in the supine (A) and lateral positions (B). Note that in the supine frontal projection the right coronary artery is largely obscured by the superimposed densely opacified aorta; the left main coronary artery (LC) and the point of bifurcation into the anterior descending (AD) and circumflex (Circ.) branches, however, are better seen than on the lateral projection. The lateral projection shows the origin and course of the right coronary artery (RC) to much better advantage than does the frontal projection, but the dense concentration of contrast material in the supravulvar region frequently obscures the proximal few centimeters of the anterior descending branch of the left coronary artery. Although the lateral projection is the best single projection to use, we have adopted simultaneous biplane techniques for more detailed study of all portions of the coronary arteries.

copy. Fortunately the nylon catheters, although small, were too stiff to permit their passage into a coronary artery, in contrast to this danger when more flexible smaller-bore ordinary cardiac catheters were used.

#### AMOUNT OF CONTRAST MATERIAL

The method which was finally adopted—of using only one rapid injection of 20 to 30 c.c. of 90 per cent Hypaque<sup>2</sup> through multiple-side-opening, closed-end nylon

<sup>2</sup> Winthrop Laboratories, New York 18, N. Y.

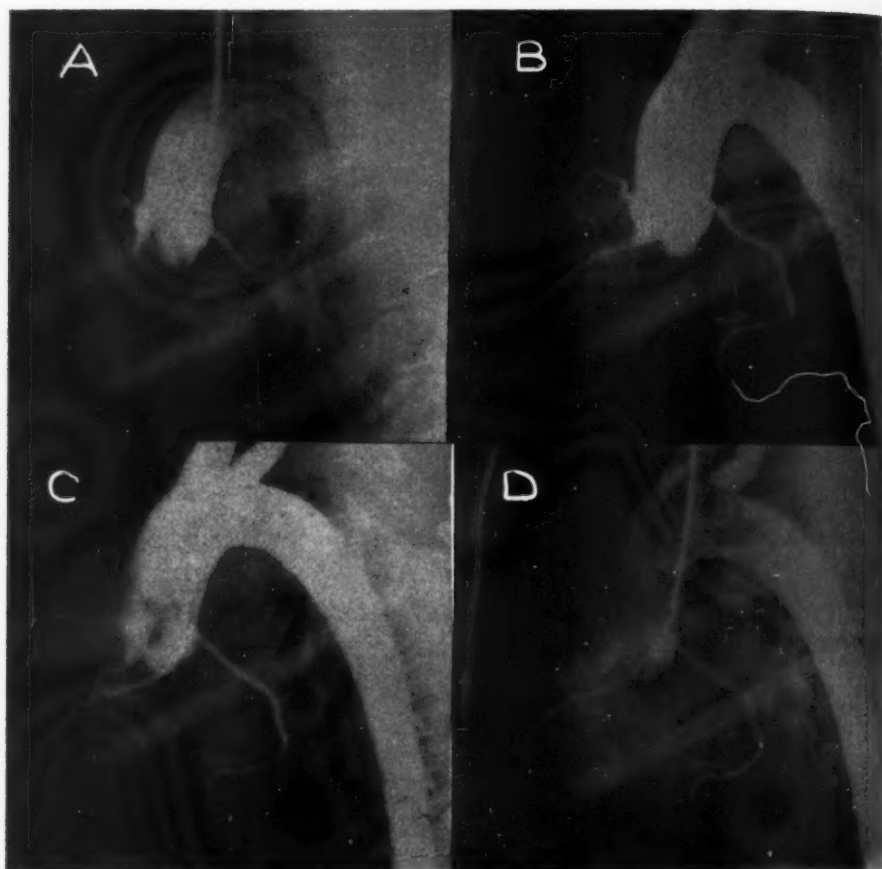


Fig. 4, A-D. A. Exposure made one second after injection began shows the aortic valve open during systole. Proximal few centimeters of both the right coronary artery (RC) and left circumflex branch (Circ.) are filled.

B. Exposure made late during the subsequent diastolic phase shows good visualization of the distal portions of all major branches of the coronary arteries; the anterior descending branch (AD) of the left coronary artery is visualized. The aorta is now completely opacified at the end of the injection.

C. Exposure made during early systolic phase: The aortic valve is beginning to open, with dilution of the concentration of contrast material in the supraventricular region due to the nonopaque blood from the left ventricle. Proximal portion of right coronary artery is beginning to lose its opacity.

D. Late during the systolic phase the nonopaque blood from the left ventricle has forced the opaque contrast material into the descending aorta. The opacity of the contrast material is diminishing in the proximal portions of all the major branches of the coronary arteries.

catheters and simultaneous biplane filming (Fig. 3)—resulted in consistently good visualization of the coronary arteries in dogs. This amount of contrast material was well tolerated by our 40-pound animals and is proportional to 112 c.c. in a 150-pound man. When such small amounts as 4 to 6 c.c. of 90 per cent Hypaque were rapidly injected, we were frequently able to get a good demonstration of the

coronary artery nearest the tip of the catheter, but visualization of the opposite artery was usually less satisfactory. We therefore concluded early in the course of our experiments that the nonocclusive method of coronary arteriography would require larger amounts of rapidly injected contrast material if good visualization of both the right and left coronary arteries was to be achieved.

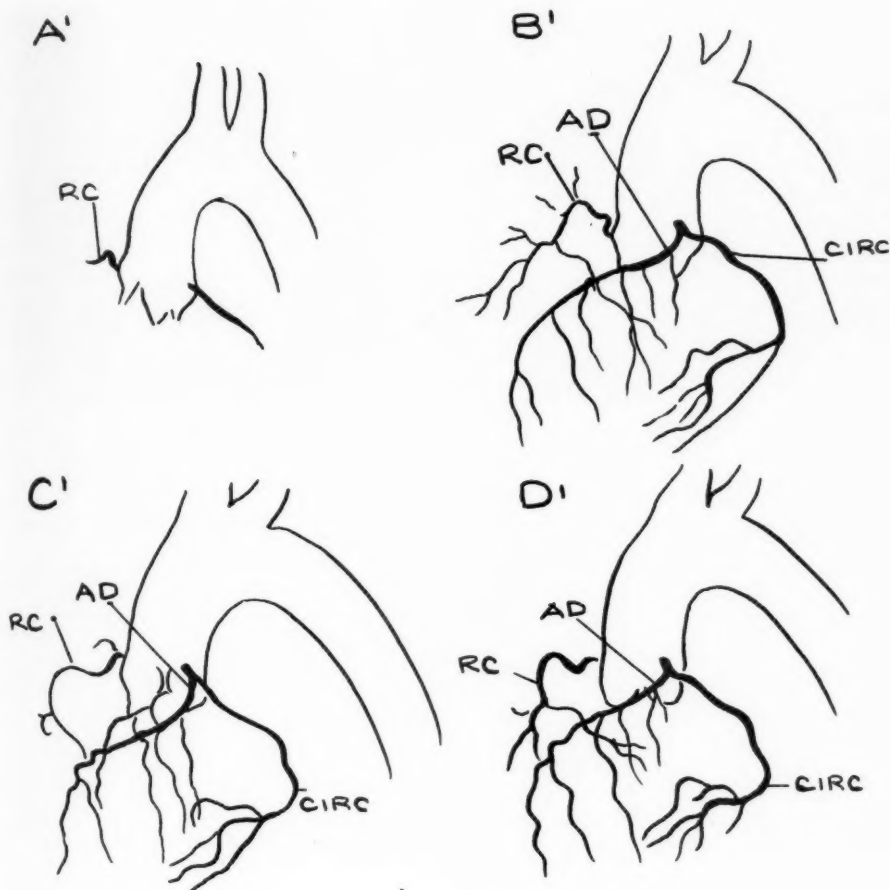


Fig. 4, A'-D'. Line drawings of A, B, C, and D.

#### TIMING OF INJECTIONS AND EXPOSURES IN RELATION TO DIFFERENT PHASES OF THE CARDIAC CYCLE

It was observed that coronary artery filling occurred primarily during diastole, although there was also evidence of significant coronary flow during systole (Fig. 4). This problem was first studied with the aid of an electrical relay circuit which could be set to activate an automatic pressure injector at any time after the peak of the first R wave following closure of the circuit (Fig. 1). A second relay circuit enabled us to initiate serial filming at any interval after the R wave which triggered the injection. We finally concluded that, with our method, it made no

real difference at what time during the cardiac cycle the injection began, and the first relay was accordingly abandoned. However, we did retain the use of a delay circuit which allowed us to begin serial filming about midway in the course of the injection. Usually, with 20 to 30 c.c. of medium, the duration of the injection was approximately one second. After 10 to 15 c.c. had been injected, the bolus of contrast material was large enough for opacification of the regions of the coronary ostia, the supravalvular region of the aorta, and the proximal portions of the coronary arteries. During the final half of the injection the bolus maintained maximum concentration in the region of

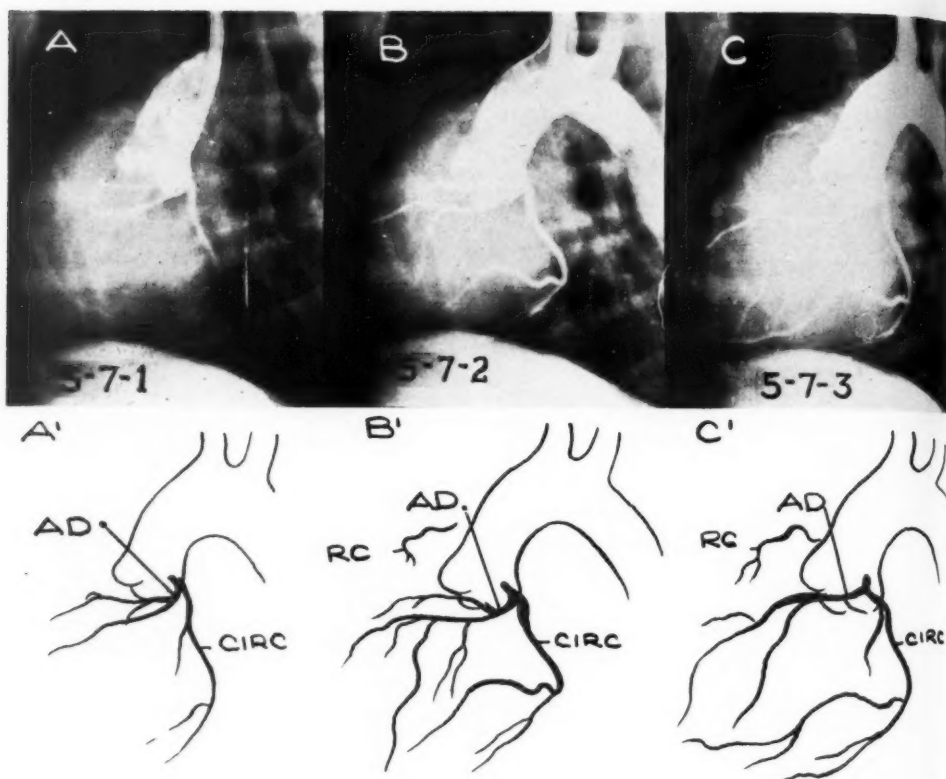


Fig. 5. Series of six exposures (three on opposite page) made in total elapsed time of three seconds, starting during a one-second injection of 20 c.c. of 90 per cent Hypaque.

A. First exposure made shortly after beginning of injection, showing filling of proximal portions of the left anterior descending (AD) and left circumflex (CIRC) branches.

B. Good filling of the proximal two-thirds of these branches.

C. Third exposure, demonstrating good filling of the entire length of the anterior descending and circumflex branches of the left coronary artery and moderately good filling of the right coronary artery (RC).

the ostia of the coronary arteries, regardless of the phase of the cardiac cycle or position of the aortic valve, and as a result there was a continuous flow of contrast material into the arteries. Thus, clearing of the aorta and coronary circulation usually began during the late part of the injection phase and was completed during the subsequent one or two seconds. It was surprising to us to learn how fleeting was the time thus available for filming the optimally opacified coronary arteries (Figs. 2, 4, and 5). In spite of this, we were consistently able to show good progressive filling on three serial films made within a period of one and one-fifth seconds during the period of maximum

concentration of the contrast material near the coronary ostia (Figs. 2, 4, 5, and 6). Opacification of the coronary arterial tree occurred in the course of two or three successive cardiac cycles, during each of which coronary visualization progressed, since the concentration of the contrast material remained at a maximum level in the region of the ostia.

#### INJECTION PRESSURE

If all other factors remained constant, the injection pressure was related directly to the speed of the injection. Many compressed-air injectors are available, our device being the Cidlund. If, during the introduction of 20 to 30 c.c. of 90 per cent



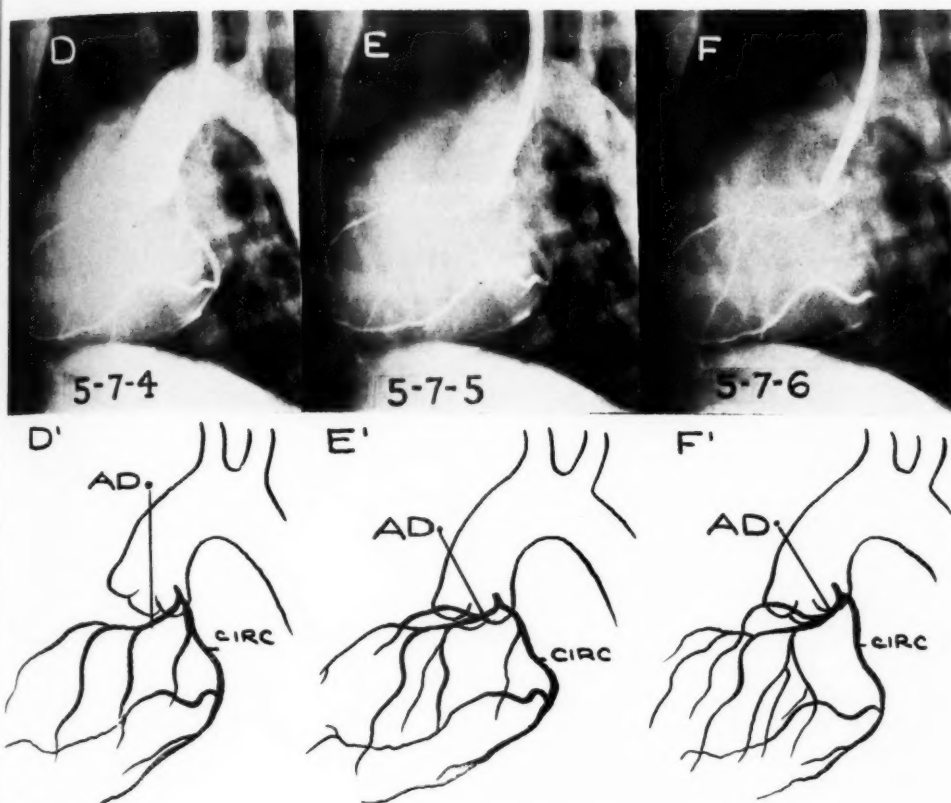


Fig. 5. D. At the time the fourth exposure was made the injection had been completed.  
 E. Fifth exposure showing clearing of the contrast material from the proximal aorta by the nonopaque blood ejected from the left ventricle. Contrast is beginning to disappear from the proximal portions of the major coronary artery branches.  
 F. Last exposure: complete clearing of the aorta. Residual contrast material is in the distal two-thirds of the anterior descending and circumflex branches of the left coronary artery. The right coronary artery is no longer seen.

Hypaque, the injection pressure was less than 5 kg./cm.<sup>2</sup>, the consequent prolongation of the injection resulted in poor opacification of the regions of the coronary ostia and nonvisualization of the coronary arteries (Fig. 7, A-G). With pressures of 6-10 kg./cm.<sup>2</sup>, it was possible to inject safely 20 to 30 c.c. of 90 per cent Hypaque in half a second to a second, with good opacification of the regions of the coronary ostia, and subsequent good visualization of the arteries (Fig. 7, H-J).

#### SEQUENCE OF FILLING OF CORONARY CIRCULATION

We were able to demonstrate regularly, with the nonocclusive method, that it

takes two to three cardiac cycles for the coronary arteries to fill completely from their origin to the smaller branches (Figs. 1, 4, and 6). When filming was initiated midway in the course of a one-half- to one-second injection of 90 per cent Hypaque, we repeatedly showed on the first serial film that the proximal third of the coronary arteries was well filled. On the second film, made six-tenths of a second later, the middle third of the vessels had filled, and on the third exposure, after an equal interval, the distal third of the coronary arterial circulation was demonstrated. Thus, in a series of three films, in an elapsed time of only one and one-fifth seconds, the first exposure being made

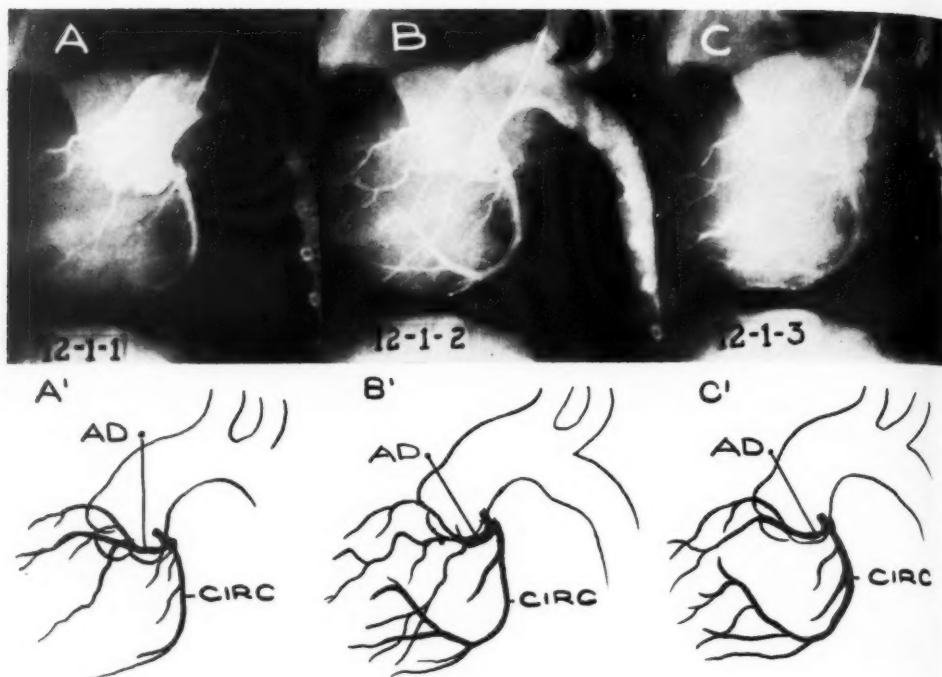


Fig. 6. Series of three consecutive exposures made in a total elapsed time of 1.2 seconds. First exposure (A) made one-half second after injection began shows good filling of the proximal portions of the left anterior descending (AD) and circumflex branches (CIRC) of the left coronary artery. Exposure made 0.6 second later (B) demonstrates further filling of the branches of the left coronary artery. Exposure C, 0.6 second after B, shows distal portions of the branches of the left coronary artery well filled.

midway during a one-second injection of 20 to 30 c.c. of a concentrated bolus of contrast material into the supravallular region, progressive filling can be clearly and regularly shown in dogs.

#### DIFFICULTY IN FILLING THE RIGHT CORONARY ARTERY IN DOGS

The right coronary artery is quite small in the dog, and we believe that this accounts in part for the difficulty in consistently visualizing this vessel by the nonocclusive method of coronary arteriography. In about 50 per cent of human beings, however, the right coronary artery is preponderant (17); in some 20 per cent there is left coronary artery preponderance, and the remaining 30 per cent have a balanced coronary circulation, without predominance of either artery. In view of these observations and the greater size of the coronary arteries, it would seem

logical to assume that better visualization of both arteries would be obtainable in man.

#### ELECTROCARDIOGRAPHIC CHANGES DURING CORONARY ARTERIOGRAPHY

Electrocardiographic tracings were obtained frequently during the injections, including the time before surgery was started, during the introduction of the catheter, immediately preceding the injection, during the injection, and at intervals varying from one minute to twenty minutes thereafter. Changes frequently occurred during the introduction of the catheter, particularly if open surgical manipulation involved the superior mediastinum, as when the surgical member of the team introduced his fingers through the incision for the purpose of guiding the large catheter originally used through the brachiocephalic artery into the ascending aorta.

## A. EKG DATA FOLLOWING 93 INJECTIONS OF ORGANIC IODINE CONTRAST MATERIALS

EKG FINDINGS FOLLOWING INJECTIONS	NO. OF TIMES NOTED	TIME REQUIRED FOR REVERSIBILITY OF CHANGES				NO. ANIMALS DEVELOPING PERMANENT CHANGE	
		Less Than 2 Minutes	2-5 Minutes	5-10 Minutes	Longer Than 10 Minutes	After 3 or Less Injections	After More Than 3 Injections
BRADYCARDIA	38	33	1	4			
DEPRESSED ST SEGMENTS	6	4	1	1			
INVERTED T-WAVE	42	20	1	4	6		6
DIPHASIC T-WAVE	2	1	12				
FLAT T-WAVE	3	3					
QRS CHANGES	6	6					
OTHER	1 (High notched T-waves)					1	
VENTRICULAR EXTRA SYSTOLES	2	2					
VENTRICULAR TACHYCARDIA	2	1	1				
VENTRICULAR FIBRILLATION	1 (Death)						
ASYSTOLE	8	8					

## B. EKG DATA FOLLOWING TOTAL OF 67 SALINE INJECTIONS, BLOOD INJECTIONS AND BAG INFLATIONS

EKG FINDINGS FOLLOWING INJECTIONS	NUMBER OF TIMES NOTED				TIME REQUIRED FOR REVERSIBILITY OF CHANGES			
	After 32 Isotonic Saline injections	After 12 Autogenous Blood injections	After 16 Bag inflations (Aortic Occlusion)	After 7 5% Glucose H <sub>2</sub> O injections	Less than 2 Minutes	2-5 Minutes	5-10 Minutes	Longer than 10 Minutes
BRADYCARDIA	28				24			4
		8			8			
			5		4			1
				3	3			
INVERTED T-WAVES	26				24			2
		7			6	1		
			7		6	1		
				5	5			
VENTRICULAR EXTRA SYSTOLES			3		3			
VENTRICULAR TACHYCARDIA			1		1			
ASYSTOLES	2				2			
		1			1			

Table I. A. Electrocardiographic effects resulting from the injection of iodized contrast materials into the supraventricular region of the aorta. B. The injection of normal saline, 5 per cent glucose in water, and the animal's own blood, caused similar changes. Inflation of the bag of the occlusive catheter produced these same nonspecific effects. The majority of electrocardiographic changes are reversible in less than two minutes.

This type of manipulation was sometimes employed early in our experiments, because of the difficulty in introducing the large catheters through the carotid arteries of small dogs. There resulted a wide spectrum of electrocardiographic abnormalities, including runs of multiple

extrasystoles, depressed ST segments, inverted T-waves, and ventricular fibrillation.

Inasmuch as mediastinal manipulation was not necessary for the passage of smaller-bore catheters, significant electrocardiographic changes were not frequently

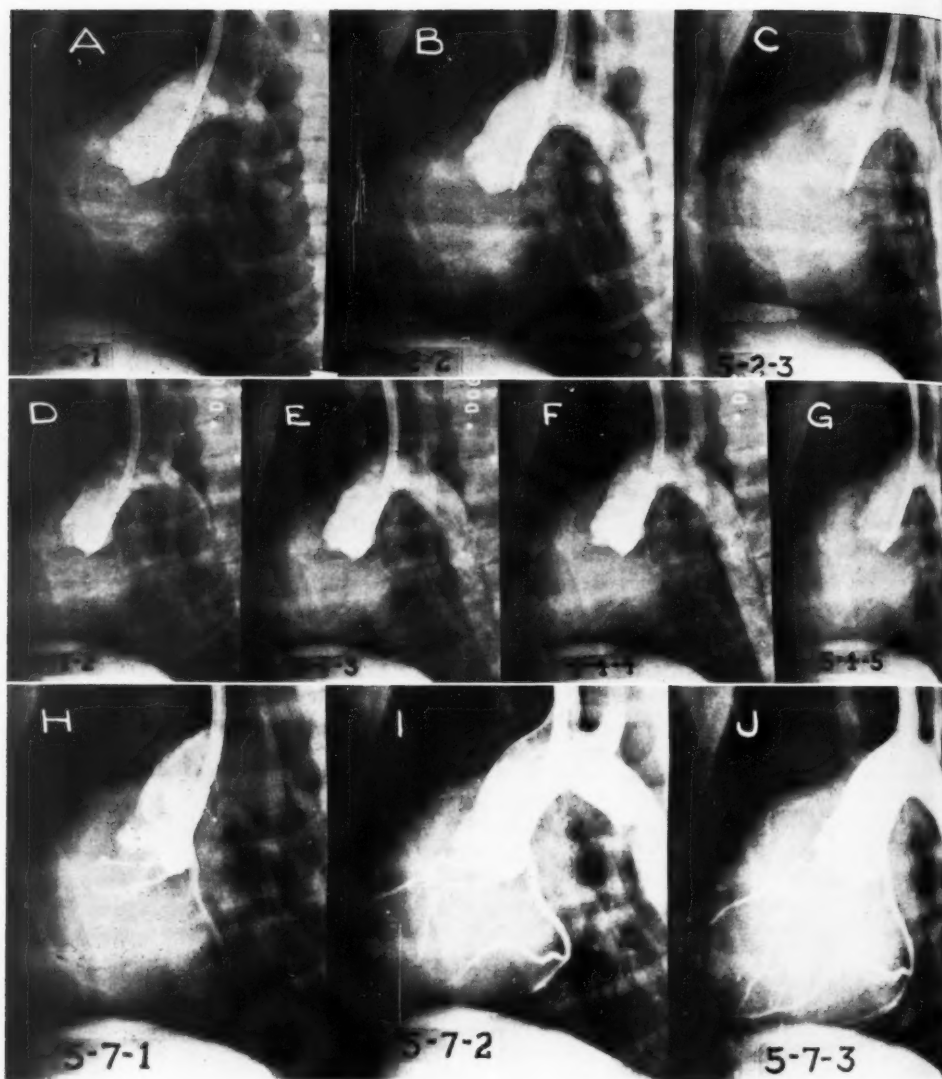


Fig. 7. A-J. Demonstration of effect of injection pressure.

A-C. Series of three consecutive exposures made in a total elapsed time of 1.2 seconds during the injection of 15 c.c. of Thorotrast. The injection pressure was 3 kg./cm<sup>2</sup>. The bolus of contrast material never reached maximum possible concentration in the proximal aorta because of the relatively small amount of contrast material delivered per second, and also because of the dilution of the contrast material by the nonopaque blood being ejected from the left ventricle.

D-G. Four consecutive exposures made in a total elapsed time of 1.8 seconds during the injection of 25 c.c. of Thorotrast. Although more contrast material was used, low injection pressures did not allow the accumulation of a concentrated bolus of contrast material in the proximal aorta. Therefore, if low injection pressures are used, the visualization of the coronary arteries is poor, regardless of the amount of contrast material used.

H-J. Three consecutive exposures made during a total elapsed time of 1.2 seconds following the rapid injection of only 15 c.c. of Thorotrast. An injection pressure of 8 kg./cm.<sup>2</sup> was used, resulting in rapid placement of a concentrated bolus of contrast material in the region of the coronary artery ostia, with better visualization of the coronary arteries.

All exposures in this figure were made on the same animal. Only the injection pressure (and therefore the speed of injection and concentration of the contrast material in the region of the coronary artery ostia) varied. The slightly different magnification factors in the different series of exposures are due to the photographic technic used.

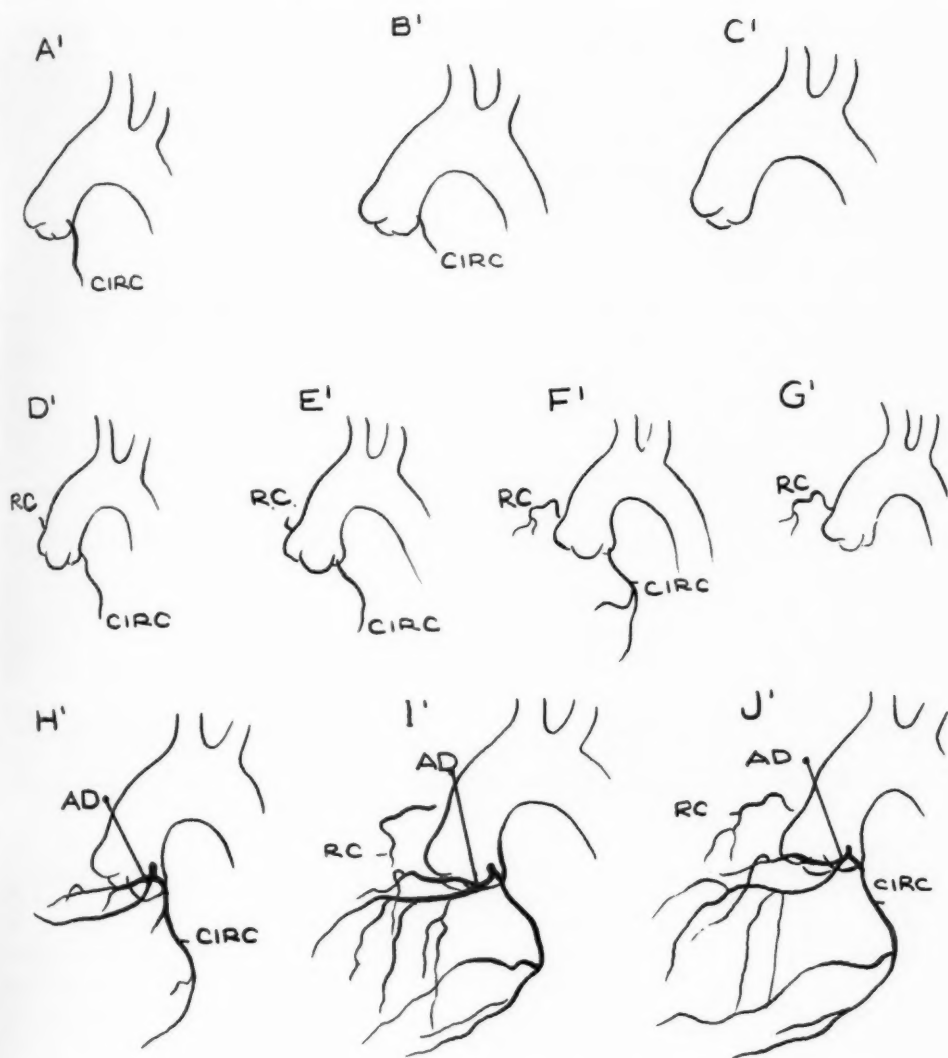


Fig. 7, A'-J'. Line drawings of A through J respectively.

noted in our later studies. Occasionally slight depression of ST segments and flattening or slight inversion of the T-waves were seen. During the injection of contrast material the electrocardiogram was usually definitely abnormal, with extrasystoles, tachycardia, brief periods of asystole, depressed ST segments, flattening or inversion of T-waves, and ventricular tachycardia (Table I). These variations were almost always transitory, with com-

plete reversion to the preinjection electrocardiogram within two to three minutes after the first two injections (Fig. 8). Multiple injections, often totaling 100 to 200 c.c. of contrast material, sometimes resulted in more permanent ST segment and T-wave changes. No permanent electrocardiographic changes were noted when the number of injections was limited to two, although the transitory deviations mentioned above were frequent. The



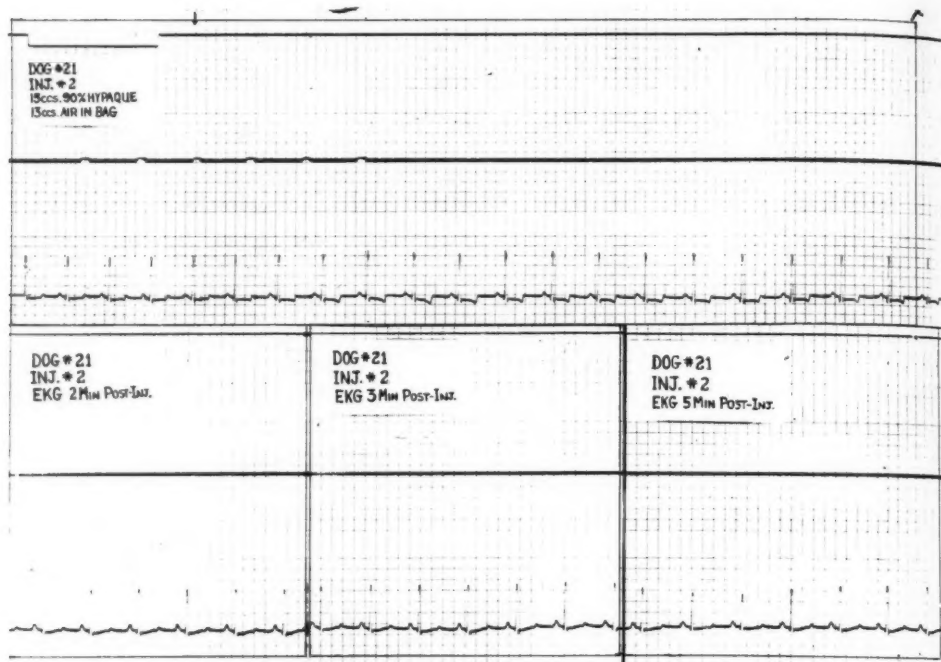


Fig. 8. Example of electrocardiographic records made before, during, and at regular intervals after the injection of contrast material. The top portion of this figure shows a gradual change from a diphasic but largely upright T-wave, to a definitely inverted T-wave after the injection of 15 c.c. of 90 per cent Hypaque. These same changes occurred in this animal whether or not the aorta was occluded. The lower recordings show reversion to the normal preinjection electrocardiographic appearance within two minutes after the injection was completed. This reversion of the electrocardiogram to the normal preinjection appearance almost always occurred.

inflation of an intra-aortic occlusion bag without injection of contrast material produced the same type of changes as did the introduction of an opaque medium (Fig. 9).

The significance of the changes in the electrocardiogram is difficult to interpret, although it must be assumed that there is a combination of factors which produce what appears to be evidence of temporary "coronary insufficiency." These factors probably include the direct effect of the contrast material on the coronary arteries, the sudden increase in the intra-aortic pressure with resultant increased workload on the left ventricle, the distention of the ascending aorta, pharmacologic effect of the contrast material reaching the vagal centers, etc. Of great interest to us was the fact that we were able frequently to produce ST-segment depression and T-

wave changes after injection of normal saline, 5 per cent glucose in water, and the animal's own blood. Inasmuch as the electrocardiographic changes were transitory, it is our opinion that the mere possibility of their occurrence in man should not preclude the attempt to save the life or improve the life-expectancy of persons with serious coronary artery disease.

#### INTRA-AORTIC PRESSURE CHANGES DURING INJECTION

During the injection of 20 to 30 c.c. of 90 per cent Hypaque in one second into the nonoccluded aorta, the supra-avalvular systolic and diastolic pressures rose, on the average, about 25 mm. Hg. The inflation of a balloon-type catheter, resulting in complete occlusion of the ascending aorta, caused a rise of 50 to 60 mm. Hg

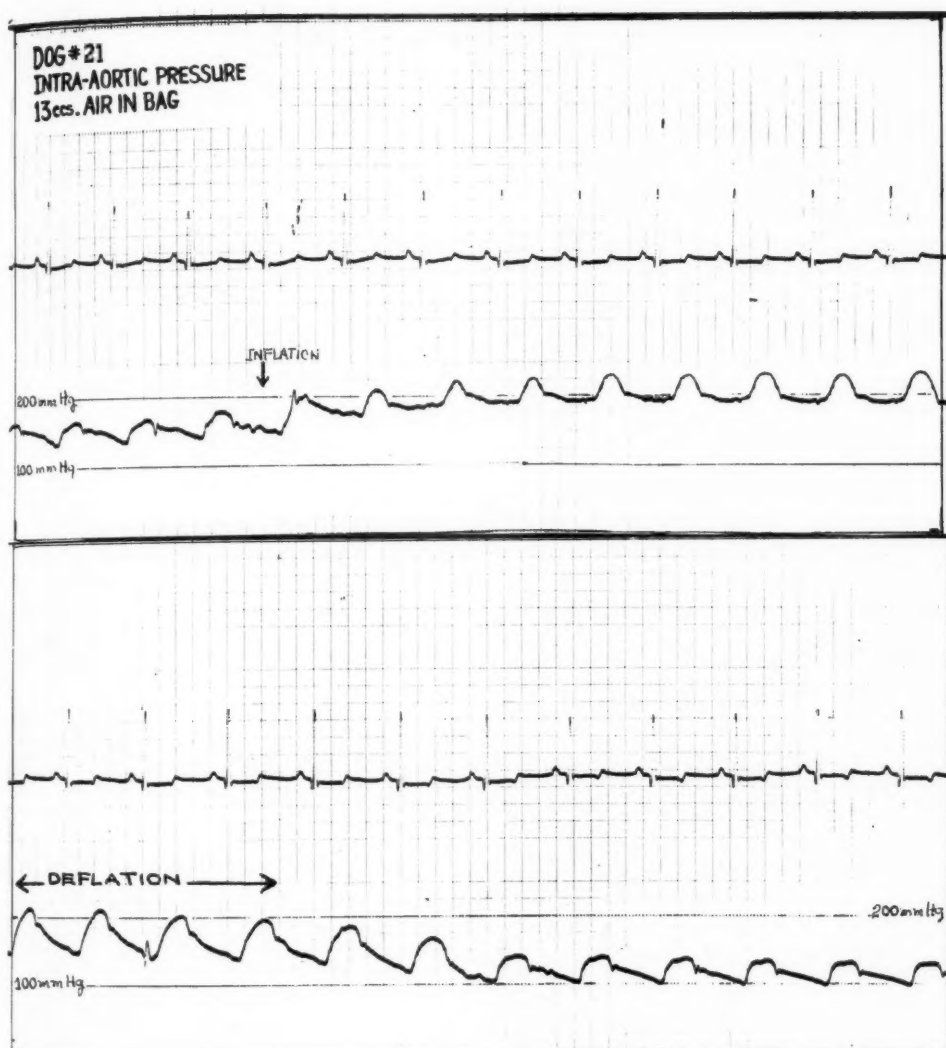


Fig. 9. Electrocardiographic and intra-aortic pressure recording made during a six-second inflation of the bag of an aortic-occlusion catheter. The intra-aortic pressure usually rose to a level approximately 50 mm. Hg above the preinflation aortic pressure. Following the deflation of the bag, the intra-aortic pressure often fell to a level 50 mm. Hg lower than the normal preinflation intra-aortic pressure. During inflation the T-waves often became diphasic, flat, or inverted. The inversion frequently became more pronounced after the bag was deflated, but these changes were almost always reversible, the electrocardiogram returning to the preinflation appearance. No explanation for the post-deflation electrocardiographic changes and intra-aortic pressure changes can be offered.

in the supravalvular systolic pressure even in the absence of any injection. (Fig. 9). Thus, when an injection was made between the occluding balloon and the aortic valve, the total systolic pressure rise there was frequently 75 to 85 mm. Hg above normal. When the aorta was oc-

cluded, the diastolic pressure usually rose to the same degree as did the systolic (Fig. 9), although in one dog the rise in systolic pressure was accompanied not by a diastolic rise, but by a resultant doubling of the pulse pressure. After the deflation of the bag, both the systolic and diastolic

pressure usually returned to the pre-inflation level, although they sometimes fell even lower (Fig. 9). The reason for this post-deflation fall is not known. Our supravalvular aortic pressure measurements were made to determine the differences with and without aortic occlusion during injection.

#### COMPLICATIONS

Seven of our 50 dogs died, all during the earlier part of our study, when the surgical technics were more traumatic because of the use of large catheters in small dogs, the necessity for open mediastinal manipulation, etc.

There were no deaths attributable to the introduction of the smaller catheters now employed, nor did any fatalities occur with injections of 20 to 30 c.c. of 90 per cent Hypaque when the number of injections was limited to three or less.

#### HUMAN CORONARY ARTERIOGRAPHY

We are now using this method of arteriography in man in suspected and known cases of occlusive disease of the coronary arteries. An account of our experience will appear in the next issue of RADIOLOGY.

#### SUMMARY

The development of a transcarotid method of coronary arteriography in dogs has been described. This affords excellent visualization of both coronary arteries in most instances and is now being used clinically in man in an attempt to help solve some vexing problems in the diagnosis and treatment of coronary artery occlusive diseases.

The following is a list of the important features of the method as developed in dogs:

1. The catheter is introduced through a tiny incision in the right common carotid artery and the tip is easily positioned in the aortic valve region without fluoroscopic control by recognition of the characteristic to-and-fro movement of the catheter as it approaches the valve region.

2. Twenty to thirty cubic centimeters

of 90 per cent Hypaque is injected in approximately one second through a closed-end, multiple-hole side-opening nylon catheter, with an outside diameter of 3.5 mm. and an inside diameter of 2.5 mm.

3. Injection pressures of 6 to 10 kg./cm.<sup>2</sup> are used.

4. Serial filming is started after 10 to 15 c.c. of the contrast material has been injected by means of an electronic relay circuit. With the Gidlund device used by us, serial simultaneous biplane filming can be started approximately midway in the course of a one-second injection of 20 to 30 c.c. of 90 per cent Hypaque.

5. Serial biplane exposures are made at the rate of three per second during a period of two to four seconds.

6. The majority of electrocardiographic changes coincident to the injection of iodine-containing contrast materials (90 per cent Hypaque and 70 per cent Cardio-grafin) into the supravalvular region of the aorta of dogs are nonspecific and quickly reversible.

7. The same type of electrocardiographic change can be induced by injecting saline, blood (the animal's own blood reinjected), and 5 per cent glucose in water or by the inflation of the bag of an aortic-occlusion catheter.

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Department of Radiology  
Ohio State University  
Columbus 10, Ohio

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## SUMMARIO IN INTERLINGUA

## Arteriographia Coronari: Disveloppamento de Un Methodo in Animales, con Attention Particular Prestate al Effectos Physiologic

In un gruppo de 50 canes bastarde, 350 injectiones esseva effectuate in le tentativa de effectuar opacification del arterias coronari. Le arteria carotic dextero-commun esseva usate como puncto de entrata pro le catheter. Isto passava allora via le trunco brachiocephalic a in le aorta ascendente. Un vigorose movimento de va-e-veni de 2 a 3 mm del parte del integre catheter indicava que le puncta esseva proxime al region del valvula.

Visualisation de qualitate uniforme-bon esseva obtenite de ambe arterias coronari con le uso de un injection de 20 a 30 cm<sup>3</sup> de 90 pro cento de Hypaque intra approximativemente un secunda, per catheteres de nylon a multiple orificios lateral e puncta claudite (diametro externe de catheter, 3,5 mm), con photographia biplan effectuate simultaneemente. Esseva usate pressioness de injection de 6 a 10 kg/cm<sup>2</sup>. Un circuito a retardo electronic permitteva expositiones biplan serial

al rhythmo de tres per secunda durante periodos de inter duo e quatro secundas a partir del momento quando le introduction del substantia de contrasto passava le nivello de 10 a 15 cm<sup>3</sup>.

Le majoritate del alterationes electrocardiographic coincidente con le injection de substantias de contrasto a contento de iodo (90 pro cento de Hypaque e 70 pro cento de Cardiografin) a in le region supravulvular del aorta canin se provava non-specific e esseva rapidamente reversibile. Alterationes del mesme typo pote esser inducite per le injection de solution salin o de un solution de 5 pro cento de glucosa o per le re-injection de sanguine ab le animal experimental mesme o per le inflation del ballon de un catheter de occlusion aortic.

Currentemente le autores utiliza le hic delineate methodo in studios arteriographic in humanos. Resultatos de iste investigation va esser reportate in le proxime numero del presente periodico.

## Some Factors Altering the Severity of Acute Radiation Pneumonitis: Variation with Cortisone, Heparin, and Antibiotics

WILLIAM T. MOSS, M.D., FRANCIS J. HADDY, M.D., and SANFORD K. SWEANY, M.D.

MOST OF US justifiably regard the lungs as relatively radioresistant. It is only when large ports are irradiated to moderately high doses that we begin to see clinical symptoms of radiation pneumonitis. Among the many known factors which influence the severity of such symptoms are the type and extent of superimposed infection, status of pulmonary function prior to this additional damage, and the general condition of the patient. Time-dose-volume factors are also important, but their relationships to radiation pneumonitis remain poorly defined, particularly in patients with pre-existing lung disease. Symptom-producing reactions will be kept to a minimum if field sizes are small and if doses are fractionated and kept as low as possible. A certain number of reactions, however, are unavoidable.

Therapy of radiation-induced lung reactions has been directed toward the decrease of fibrosis with steroids and the control of superimposed infections with antibiotics. The effects of these agents have been difficult to evaluate clinically, chiefly because of the highly variable course of the primary disease.

In our previous study (9), whole chest irradiation was found to produce a striking reduction of total thoracic compliance, *i.e.*, relation of pressure to volume. The decrease progressed for at least nine to twelve months following irradiation. Compliance of the thoracic cage changed very little; nearly all of the change in total compliance was due to the change in lung compliance. It thus appears that total thoracic compliance may serve as a

measure of the lung damage produced by irradiation. In the present study this parameter was used to investigate the effectiveness of several agents in altering radiation-induced lung changes.

### METHODS

Female Sprague-Dawley rats weighing 150 to 175 grams were anesthetized with 4 mg. of sodium pentobarbital intraperitoneally. The whole chest was irradiated through a single anterior port. All radiations were given with the 220-kvp Picker x-ray therapy machine (T. S. D., 37 cm. filter, 0.5 mm. Cu + 1 mm. Al, h. v. l. 0.9 mm. Cu; 48 r/min.). Dose-time factors were varied as indicated in the section on results. Nonirradiated control animals were allowed to age with irradiated experimental animals.

The relation of pressure to volume in the thorax was studied at intervals with the rat anesthetized and curarized. Immediately after anesthesia and injection of 10 mg. of succinylcholine intraperitoneally, a tracheostomy was made. A polyethylene tube was tied into the trachea and attached to a rat respirator. Paralysis followed in three to four minutes. Artificial respiration was then stopped and, after thirty seconds, lung volume was rapidly increased in 1-ml. increments with a tuberculin syringe. Endotracheal pressure was continuously measured with a resistance wire pressure transducer and a direct writing recorder. After a rest period of twenty to twenty-five seconds, the test was repeated. The pressures were averaged in order to construct individual pressure-volume curves.

<sup>1</sup> From the Departments of Radiology and Medicine, Northwestern University School of Medicine, and Veterans Administration Research Hospital, and the Department of Therapeutic Radiology, Chicago Wesley Memorial Hospital, Chicago, Ill. This work was supported in part by the U. S. Public Health Service, Grant C-4354 (CI).

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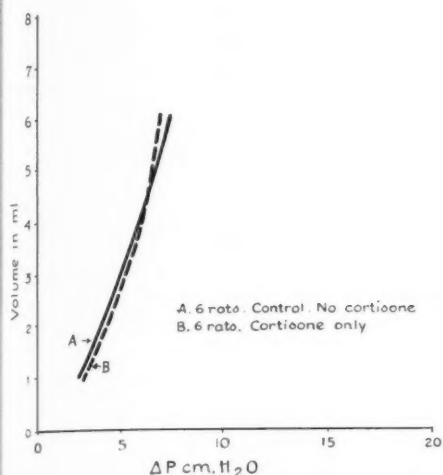


Fig. 1. Effect of prolonged cortisone administration on total thoracic compliance in unirradiated rats.

### RESULTS

**Group I. Effect of Prolonged Cortisone<sup>2</sup> Administration on Total Thoracic Compliance in Unirradiated Rats:** Naturally occurring low-grade chronic lung infections are known to exist in most rat colonies. It seemed pertinent, therefore, to study the effect of cortisone on unirradiated rats before investigating its effect on irradiated animals. Female rats of 150 to 175 gm. were distributed randomly into two groups. One group received 2.5 mg. of cortisone intramuscularly daily for thirty days. The other group received no medication. Neither group was irradiated. The relation of pressure to volume in each rat was studied after the thirty-day period. Average curves for each of the two groups are presented in Figure 1.

**Group II. Effect of Prolonged Cortisone Administration on Acute Radiation Pneumonitis:** Female rats of the size specified above were divided into three groups. One group was allowed to age without irradiation or cortisone. A second group was given 2,600 r whole-chest irradiation in three weeks through an anterior port but did not receive cortisone. A third group received a similar dose of radiations and 2.5 mg. of cortisone intramuscularly daily

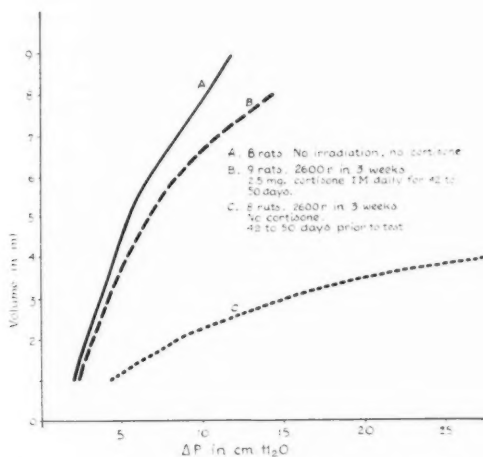


Fig. 2. Effect of prolonged cortisone administration on acute radiation pneumonitis.

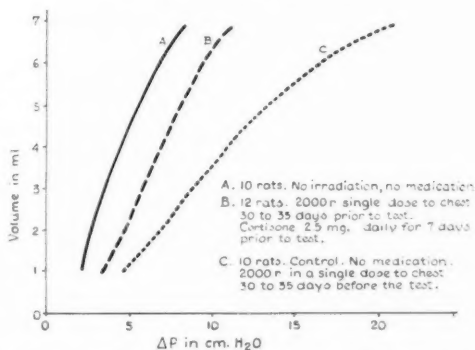


Fig. 3. Effect of cortisone given daily for seven days beginning after the onset of acute radiation pneumonitis.

from the beginning of irradiation to the end of the experiment, forty-two to fifty days later. The relation of pressure to volume was then studied in the three groups (Fig. 2).

**Group III. Effect of Cortisone Given Daily After Onset of Acute Reaction:** The experiment described in Group II was repeated except that cortisone was given for one week beginning three to four weeks after single-dose whole-chest irradiation of 2,000 r. Observations were made thirty to thirty-five days after irradiation (Fig. 3).

**Group IV. Effect of Heparin Administration on Acute Radiation Pneumonitis:** The experiment described in Group II was

<sup>2</sup> Cortisone was supplied by Schering Corporation.

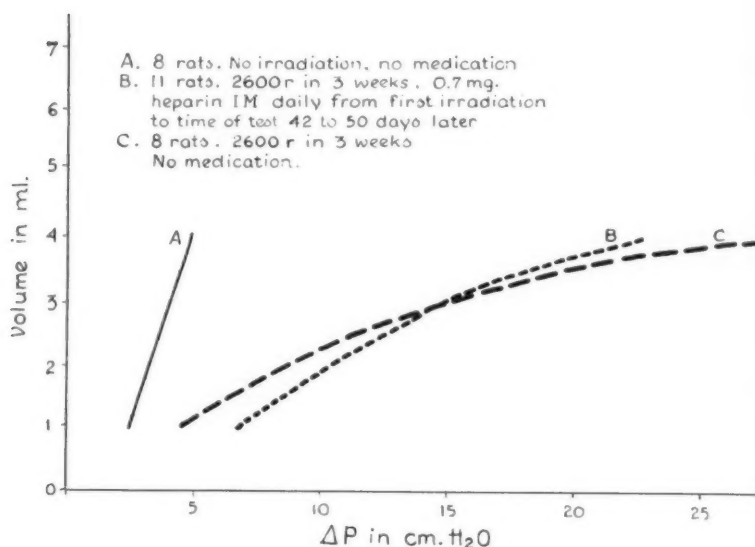


Fig. 4. Effect of heparin administration on acute radiation pneumonitis.

repeated except that, instead of cortisone, 0.7 mg. heparin<sup>3</sup> was injected intramuscularly daily from the day of irradiation to the end of the experiment (forty-two to fifty days). The results are presented in Figure 4.

**Group V. Effect of Antibiotics<sup>4</sup> on Acute Radiation Pneumonitis:** Female rats ranging in weight from 150 to 175 grams were divided randomly into two groups. Both groups were given 2,000 r single dose whole-chest irradiation. One group received no medication. The other group was given 2,000 units penicillin and 2.5 mg. streptomycin, intramuscularly, daily beginning three weeks after irradiation. In addition, 2.5 mg. tetracycline was administered intramuscularly twice each day. After seven days of this therapy, the relation of pressure to volume was studied (Fig. 5).

#### DISCUSSION

These studies show that cortisone significantly antagonizes the reduction in total thoracic compliance produced by

irradiation. The effect was most striking after one month of therapy but was noticeable even in seven days. Heparin was without effect. A combination of penicillin, streptomycin, and tetracycline gave questionable benefit.

Cortisone therapy for both acute and chronic radiation pneumonitis has been the subject of numerous studies (2-5, 7, 8, 10, 11). During the acute phase cortisone has been reported to suppress peribronchial infiltrations. One author (2) thought that this lowered the incidence of focal atelectasis, which in turn decreased fibrosis. Cortisone, however, did not alter survival when doses of whole chest radiations were high (3,000 r single dose). Rubin *et al.* (8) and Whitfield (10,11) also reported that administration of cortisone during the acute phase provided partial protection. Our findings support these conclusions relative to the acute phase. Indeed, the protection was greater than had been anticipated from the studies of others. The anatomical and microscopic changes produced will be the subject of a subsequent publication.

In contrast, there is rather general agreement that long standing radiation fibrosis is not significantly altered by

<sup>3</sup> Heparin was supplied by the Upjohn Company, Kalamazoo, Mich.

<sup>4</sup> Streptomycin and penicillin were supplied by Eli Lilly & Co., Indianapolis, Ind.

cortisone administration. Since our animals were killed thirty to fifty days after irradiation, we obtained no data relative to the therapy of established fibrosis. Subjective improvement might be expected in all types of radiation pneumonitis for two reasons. First, a feeling of well-being is nearly always associated with such therapy. Second, TSH secretion is suppressed and  $O_2$  requirements are subsequently reduced. As a result dyspnea from lung damage may be less severe.

Prolonged cortisone therapy in unirradiated rats might be expected to suppress fibrotic lung changes produced by pulmonary infections which occur naturally in most rat colonies. However, no such suppression of compliance change was observed during the relatively short period of our experiment. Compliance changes induced by irradiation, on the other hand, were strikingly suppressed. Since the measurements were made forty-two to fifty days after irradiation, we have regarded these as a part of the acute reaction. When cortisone therapy was started three weeks after irradiation and after lung changes were obvious, benefit was less striking. The degree of epilation was not altered by the drug.

The mechanism of cortisone effect during late acute and early fibrotic reactions probably is the same as anti-inflammatory responses elsewhere in the body, namely, suppression of connective tissue reactivity resulting in decreased cellular infiltration and fibrosis. Beneficial results have been reported following cortisone therapy of pulmonary fibrosis from many causes, and there is no reason to believe that the effect upon radiation-induced fibrosis and infiltration is different. It is rather surprising that so little benefit follows cortisone administration in the late phase.

Anticoagulants, such as heparin and Dicumarol, have also been reported to decrease the severity of radiation-induced lung reactions (1, 6). Heparin, however, given daily from the time of irradiation to the end of the experiment (forty-two to fifty days) failed to alter the compliance

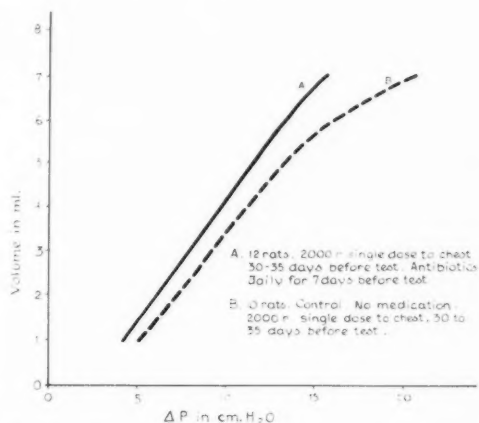


Fig. 5. Effect of antibiotics on acute radiation pneumonitis.

changes, nor did it alter the degree of epilation. We have no explanation of the discrepancy between our results and those reported by others. Whitfield and Bond failed to obtain benefit from anticoagulant administration.

There are few radiation reactions benefited by antibiotics. These agents are useful only when concurrent infection plays a significant role. The pathogenesis of radiation pneumonitis has generally been thought to include infection in the irradiated lung. Clinically, toxic symptoms occur compatible with this concept, and patients are usually placed on antibiotics with a view of diminishing the severity of infection. The fact that the course is slow and quite variable has made an evaluation of antibiotics difficult. Our study suggests that under the conditions of the experiment antibiotics were of questionable value in decreasing the functional sequelae of lung irradiation in rats. Perhaps other phases of the reaction would be more favorably influenced. The late part of the acute phase was selected for study because it seemed to be the phase most likely complicated by infection.

#### SUMMARY

The effect of steroids, heparin, and antibiotics upon radiation lung damage was

studied in rats. Total chest compliance, the relation of pressure to volume, was selected as the measure of damage. Irradiation decreased compliance. This change was unaffected by heparin but was questionably prevented by antibiotics. Cortisone definitely reduced the severity of acute radiation-induced lung damage.

Chicago Wesley Memorial Hospital  
250 E. Superior St.  
Chicago 11, Ill.

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#### SUMMARIO IN INTERLINGUA

#### Factores Que Altera le Severitate de Acute Pneumonitis de Radiation: Variation con Cortisona, Heparina, e Antibioticos

Le effecto de steroides, de heparina, e de antibioticos super le damnificationes radiatori del pulmones esseva studiate in rattos. Le compliantia thoracic total (i.e. le relation de pression a volumine) esseva seligite como mesura del damnification.

Le irradiation reduceva le compliantia. Iste alteration non esseva afficite per heparina. Illo esseva prevenite questionabilmente per antibioticos. Cortisona definitemente reduceva le severitate de acute pneumonitis per radiation.

# The Relationship Between Oxygen Tension of Inhaled Gas and the Severity of Acute Radiation Pneumonitis

WILLIAM T. MOSS, M.D., and FRANCIS J. HADDY, M.D.

THE RELATIONSHIP between oxygen tension of inhaled gas and the severity of radiation response has been studied for many tissues. Within limits, an increase in oxygen tension of the gas has been shown to increase radiosensitivity of tissues while a decrease diminishes their radiosensitivity (2, 3, 4, 7). In a comparison of various tissues, the change in sensitivity has been found not to be of the same magnitude, though it has always been in the same direction. Prior to this investigation we had no reason to believe that lung parenchyma differed from other tissues which have been studied.

In our previous work (5, 8), it was found that total thoracic compliance was a good index of the severity of radiation-induced lung damage. The test is simple to perform and it provided the data for this study. The anatomical and microscopic changes in the lungs and adrenals will be the subject of a future publication.

## METHODS

Female Sprague-Dawley rats weighing 150 to 175 gm. were anesthetized with 4 mg. of sodium pentobarbital intraperitoneally. Three rats at a time were placed in a chamber into which and from which gas flow was easily controlled. The pressure in the chamber could be varied from subnormal levels to at least three atmospheres. After adjustment of flow and pressure to produce the desired oxygen tension, the whole chests of the rats were irradiated to 2,000 r (skin) through a single anterior port. All radiations were given with the 220-kvp Picker x-ray therapy machine (T.S.D. 37 cm.; filter 0.5 mm. Cu and 1 mm. Al; h.v.l. 0.9 mm. Cu; 48 r/min.).

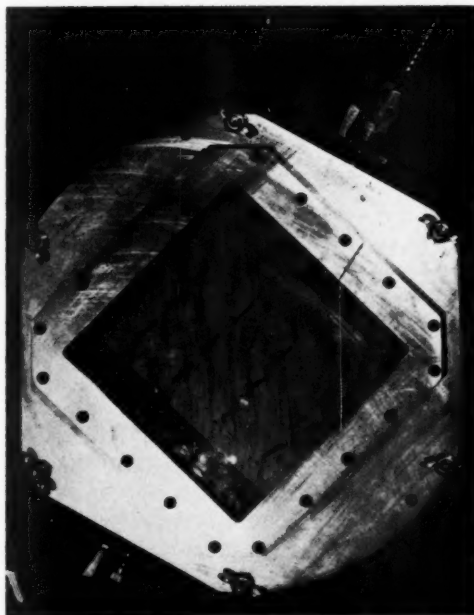


Fig. 1. Chamber with viewing window permitting the irradiation of three rats at any desired pressure and oxygen tension.

The technic of measuring compliance has been described previously (5).

## RESULTS

*Group I. Effect of Transient Changes in Inhaled O<sub>2</sub> Tensions on Subsequent Lung Compliance:* Abundant data have been accumulated showing that dissolved tissue O<sub>2</sub> influences the severity of radiation reaction. Prior to such studies on lung tissue, we decided to see if transient elevations in pressure *per se*, of the type to be used in future studies, altered compliance. Rats were distributed randomly into two groups and anesthetized with sodium pentobarbital. One group was then placed in a

<sup>1</sup> From the Departments of Radiology and Medicine, Northwestern University School of Medicine, and Veterans Research Hospital, and the Department of Therapeutic Radiology, Chicago Wesley Memorial Hospital, Chicago, Ill. This work was supported in part by the U. S. Public Health Service, Grant C-4354(C1).

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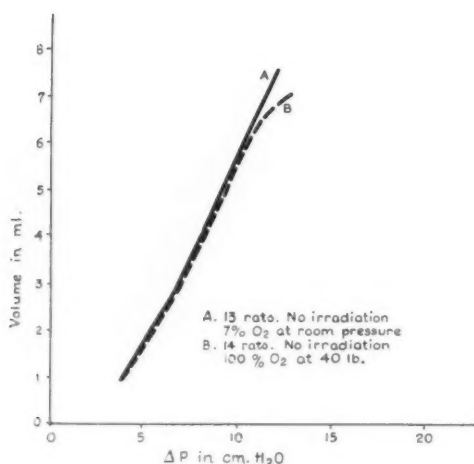


Fig. 2. Effect of transient changes in inhaled oxygen tension on subsequent lung compliance. No radiation was given to these animals.

pressure chamber (Fig. 1), the chamber was flushed with 100 per cent  $O_2$ , and the pressure was then raised to 40 lb./sq. inch in five minutes. The animals were maintained at this pressure for 41.6 minutes. This is the time which would have been required to deliver 2,000 r whole-chest irradiation, but no irradiation was given. The second group of rats was placed in the chamber and maintained for 41.6 minutes in a mixture of 7 per cent  $O_2$  and 93 per cent nitrogen at atmospheric pressure; no irradiation was given. Thirty days later pressure-volume curves were obtained for both groups (Fig. 2). Skin reactions were the same in the two groups.

**Group II. Effect of Change in Inhaled  $O_2$  Tension on the Severity of Acute Radiation Pneumonitis:** Rats of the type described in Group I were divided randomly into three groups and each group was given a single dose of 2,000 r whole-chest irradiation while in the chamber. During irradiation one group was maintained at 7 per cent  $O_2$  + 93 per cent  $N_2$  at atmospheric pressure; one group was allowed to breathe room air; and one group was maintained with 100 per cent  $O_2$  at 40 lb./sq. inch pressure. Compliance was studied in the three groups thirty to thirty-five days later. Because the results were not those

anticipated, the entire experiment was repeated. The results of the first experiment were confirmed, and the data from the two experiments were pooled (Fig. 3). Skin reactions consisted of a barely perceptible desquamation in the first group, a dry epilation in the second group, and a moist desquamation in the third group.

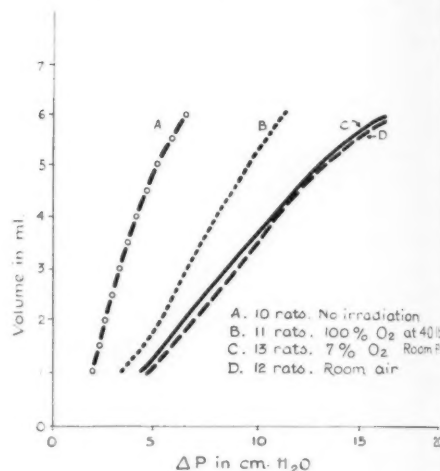


Fig. 3. Effect of changes in inhaled oxygen tension on the severity of acute radiation pneumonitis. Groups B, C, and D received 2,000 r whole-chest irradiation. No irradiation was given to Group A. Composition of inhaled gas as shown.

**Group III. Effect of Change in Pressure of Inhaled Gas on Severity of Acute Radiation Pneumonitis:** The results obtained in Groups I and II did not rule out the possibility that 40 pounds of pressure *per se* during irradiation influences radiation response. The following study was made in an attempt to evaluate the significance of increased pressure, of itself, on radiosensitivity. The experiment described in Group II was repeated with the same dose of radiations, but the oxygen tension in inhaled gas was kept constant as the pressure varied in two groups of animals during irradiation. Thus, one group breathed room air at atmospheric pressure during irradiation and one group breathed 8.4 per cent  $O_2$  in 91.6 per cent  $He_2$  at 37 pounds of pressure. The oxygen tension in the two groups was the same. Helium was used in this experiment to avoid the

bends. A single dose of 2,000 r to the whole chest was given. Total thoracic compliance was measured thirty to thirty-five days later (Fig. 4). Skin reactions in the two groups were equal.

**Group IV. Adrenal Weights After Whole Chest Irradiation—Oxygen Tension in Inhaled Gas Varied:** The unexpected results obtained in Group II, together with the supporting evidence obtained in Groups I and III, suggested that some heretofore unrecognized intrinsic factor or factors might be altering the severity of lung response. With our knowledge that cortisone can decrease the severity of the reaction (5), it was decided to repeat the irradiation described in Group II and to measure adrenal stimulation produced by this trauma by weighing adrenals at various intervals thereafter (Table I).

TABLE I: AVERAGE ADRENAL WEIGHT AND AVERAGE ADRENAL WEIGHT IN MG./100 GM. BODY WEIGHT AT VARIOUS INTERVALS AFTER 2,000-r WHOLE-CHEST IRRADIATION

(Oxygen tension of inhaled gas varied as shown)			
	10 Days	20 Days	30 Days
84% O <sub>2</sub> at room pressure	8 Rats, av. weight 61.1 mg.; 35.6 mg./100 gm.	7 Rats, av. weight 56.9 mg.; 30.6 mg./100 gm.	9 Rats, av. weight 66.1 mg.; 28.9 mg./100 gm.
100% O <sub>2</sub> at 40 lb. pressure	10 Rats, av. weight 67.1 mg.; 45.2 mg./100 gm.	6 Rats, av. weight 62.0 mg.; 35.7 mg./100 gm.	8 Rats, av. weight 67.9 mg.; 41.0 mg./100 gm.

Note: Precautions were taken to minimize the cage effect. Fat was carefully trimmed from the adrenals and they were weighed eight days after fixation in 10 per cent formaldehyde. In nonirradiated rats adrenals weighed 27 mg./100 gm. body weight after ten days and 30 mg./100 gm. body weight after thirty days.

#### DISCUSSION

These studies confirm the observation that increasing O<sub>2</sub> tension in the inhaled gas dramatically increased the severity of skin reactions. With 7 per cent O<sub>2</sub> (atmospheric pressure) in the inhaled gas, 2,000 r single-dose whole-chest irradiation usually produced a barely perceptible epilation. With 100 per cent O<sub>2</sub> at 40 pounds of pressure, 2,000 r single-dose whole-chest irradiation produced a severe moist reaction.

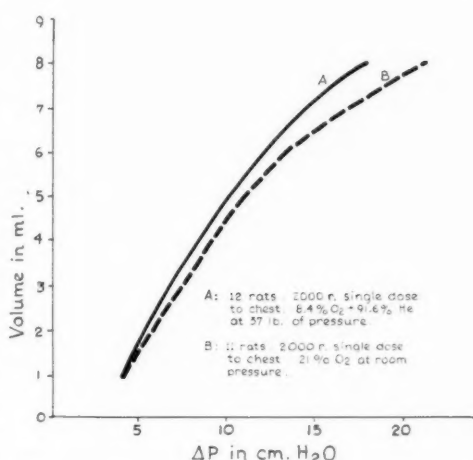


Fig. 4. Effect of maintaining oxygen tension in inhaled gas constant while varying gas pressure during period of irradiation.

Paradoxically, the lung compliance was changed less by irradiation at the higher O<sub>2</sub> tension. Pressure *per se*, as employed to increase O<sub>2</sub> tension, had no significant effect on severity of reaction.

Previously we were able to show that cortisone administered following irradiation decreases the severity of radiation-induced lung changes (5). Endogenous cortisone is known to increase as a result of adrenal response to the stress created by large-port, high-dose irradiation. This is a nonspecific response (1, 6). In Table I we see that adrenals were heavier in those animals irradiated during inhalation of O<sub>2</sub> at higher tensions. The increase in adrenal weight preceded maximum skin reaction, suggesting that other injured tissues were also contributing to the stress.

To our knowledge, there is no exception to the rule that an increase of dissolved O<sub>2</sub> in tissue above the normal results in enhanced radiosensitivity. We do not believe lung parenchyma to be an exception. It seems likely that a given increase in oxygen tension in the inhaled gas produces a smaller increase in radiosensitivity of lung than in most other tissues. The radiosensitivity of the skin and bone marrow increased seriously at the higher oxygen tensions. The findings in Group

IV animals (Table I) suggest that the more severe skin and possibly marrow reactions stimulate the adrenals and thus made available more endogenous cortisone for suppressing lung changes. We believe this may be the mechanism of the apparent decrease in lung damage in those animals irradiated at higher  $O_2$  tensions.

#### SUMMARY

Lung compliance is decreased by radiations. The change is less severe if the animal is irradiated at high  $O_2$  tensions. It was also found that the adrenals were heavier in the high  $O_2$  group than in the low  $O_2$  group. It is suggested that the severe skin and marrow reaction produced in the high  $O_2$  group results in adrenal hyperplasia with the increased production of endogenous cortisone and the subsequent suppression of compliance changes.

NOTE: We wish to express our appreciation to Miss Sandra Gold for her technical assistance in this study.

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Chicago Wesley Memorial Hospital  
250 E. Superior St.  
Chicago 11, Ill.

#### SUMMARIO IN INTERLINGUA

#### Le Relation Inter le Tension de Oxygenio in le Inhalato e le Severitate de Acute Pneumonitis de Radiation

Ha essite monstrate que in rattos le complientia pulmonar (i.e. le relation de pression a volumine) es reducite per radiation. Le reduction es minus sever si le animal es irradiate a alte tensiones de oxygenio e le adrenales esseva plus pesante que in le gruppo a basse tension de

oxygenio. Es proponite que le forte reaction cutanee e medullari que es producite in le gruppo a alte tension de oxygenio resulta in hyperplasia adrenal, con un augmento del production de cortisoma endogene e le subsequente suppression de alterationes del complientia.

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## Intracranial Posterior-Fossa Tumors<sup>1</sup>

SAMUEL B. HAVESON, M.D.

THE RADIOLOGIC diagnosis of an expanding lesion in the posterior fossa requires: (a) skillful application of the technics of plain skull roentgenography, encephalography, ventriculography, and vertebral angiography, and (b) correct interpretation of results obtained from one or more of these examinations in the individual case. The various studies should complement rather than compete with one another, and frequently a combination of all available procedures is necessary for a conclusive preoperative or antemortem diagnosis. Emphasis, however, is placed on the use of encephalography and ventriculography in evaluation of posterior-fossa tumors since, in most instances, the final result depends to a large extent on pneumographic studies.

### TECHNICAL ASPECTS OF ENCEPHALOGRAPHY AND VENTRICULOGRAPHY

Fractional encephalography is performed in the manner described by Lindgren (7). A detailed presentation of his method is beyond the scope of this paper but a few points may be outlined. The posterior fossa is examined initially with the patient sitting and the head slightly flexed. Lateral, postero-anterior, and half-axial postero-anterior films are obtained at right angles to one another without change in head position during the exposure. A Lysholm skull apparatus is invaluable for this purpose, since the x-ray tube can be moved in any direction and the central ray can be accurately directed to secure necessary projections. Prior to each of the first four exposures, from 5 to 7 c.c. of air is injected into the lumbar subarachnoid space, a total of approximately 25 c.c. being eventually introduced in the average case. Ventricular filling is accomplished by slow injection with the

head slightly flexed, and cisternal filling occurs during rapid injection with the head extended or steeply flexed. No cerebrospinal fluid is removed until after the initial films have been reviewed by the radiologist. Thus, air filling of fluid-distended spaces is easily achieved, and the increased pressure in the subarachnoid space will prevent downward cerebellar tonsillar herniation (a rather common finding in posterior fossa tumors) or, if it is already present, will keep it from increasing. If the cerebellar tonsils are observed in the subarachnoid space below the foramen magnum after the first 7 c.c. of air has been introduced, the examination is terminated without further air injection or fluid removal. Fractional encephalography is completely controlled by the radiologist, permitting an accurate detailed examination of the ventricles and subarachnoid cisterns. The study in this respect alone is certain to be superior to one in which a large air-fluid exchange is performed and a predetermined routine set of films is taken by an x-ray technician.

Successful use of ventriculography in posterior-fossa tumors depends obviously on visualization of the aqueduct and fourth ventricle. This is accomplished by filling the third ventricle with an adequate amount of air so that the aqueduct and fourth ventricle are well outlined when brought into the correct position. Air enters the third ventricle when the head is extended with the patient supine. Rapid turning of the patient into the prone position will then result in aqueductal and fourth ventricular filling in almost every case (8, 13). Repetition of the maneuver may be necessary before adequate information is obtained. When a gross symmetrical hydrocephalus is encountered on the initial supine films at ventriculog-

<sup>1</sup> From the Department of Radiology, University of California School of Medicine, San Francisco, Calif. Accepted for publication in October 1959.

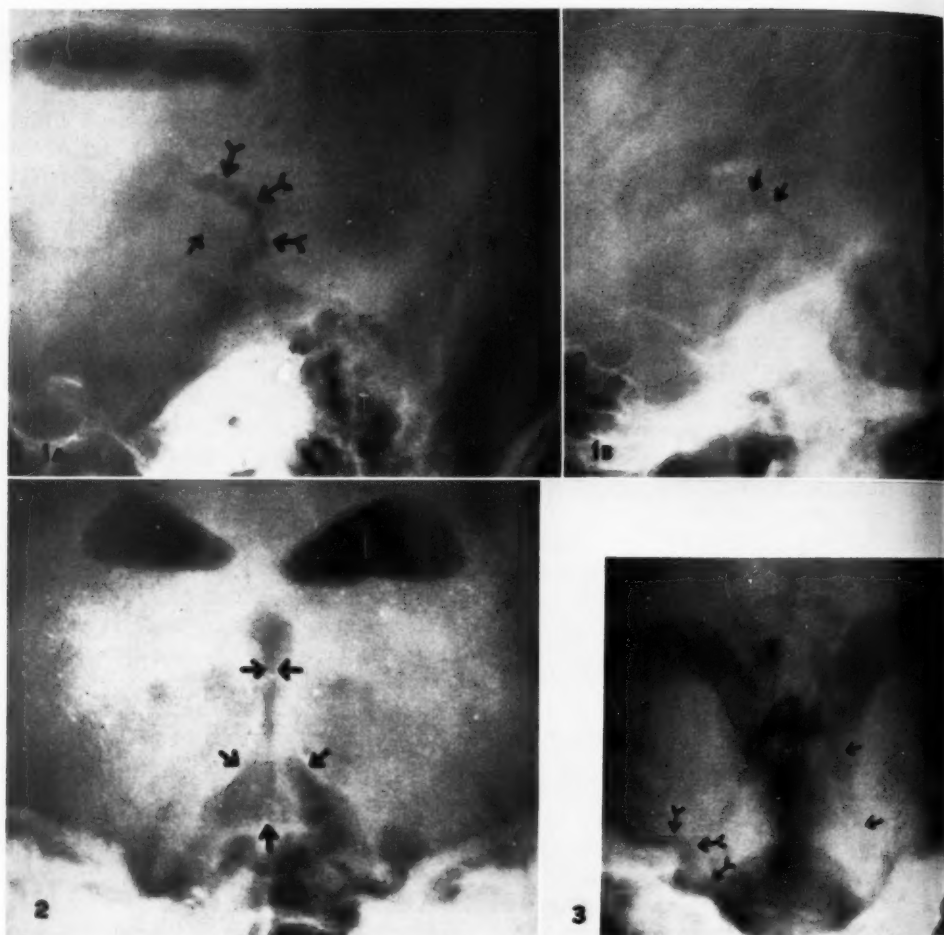


Fig. 1. A. Aqueduct with normal kink ( $\rightarrow$ ). Simultaneous filling of the cistern over the quadrigeminal plate ( $\bullet \rightarrow$ ). The slight kink occurs in the middle of the quadrigeminal plate.

B. The aqueduct forms a gentle arch ( $\rightarrow$ ) between the third and fourth ventricles.

Fig. 2. Midline position of the normal fourth ventricle (lower arrows) and aqueduct (upper arrows).

Fig. 3. The normal ambient cistern ( $\rightarrow$ ), surrounding the brain stem, and cerebellopontine angle cisterns ( $\bullet \rightarrow$ ).

raphy, the examination is not considered completed until the posterior third ventricle and posterior-fossa structures have been thoroughly examined.

#### NORMAL ROENTGEN ANATOMY

The roentgenologic appearance of the normal aqueduct, fourth ventricle, and posterior-fossa cisterns has been thoroughly described (3, 5, 11).

Lindgren and Di Chiro (5), in a study of 300 normal encephalograms, showed that in 65 per cent a kink existed between the

superior and inferior colliculi of the quadrigeminal plate (Fig. 1, A); in 35 per cent the aqueduct formed a gentle arch between the third and fourth ventricles (Fig. 1, B). Exaggeration of the normal kink or increase in the normal arch is an important localizing sign in expanding lesions of the posterior fossa. The aqueduct and fourth ventricle are normally in the midline on frontal views (Fig. 2). Their forward or backward displacement can be measured on lateral films by Twining's point (13), Lysholm's point (8), or the ventricular

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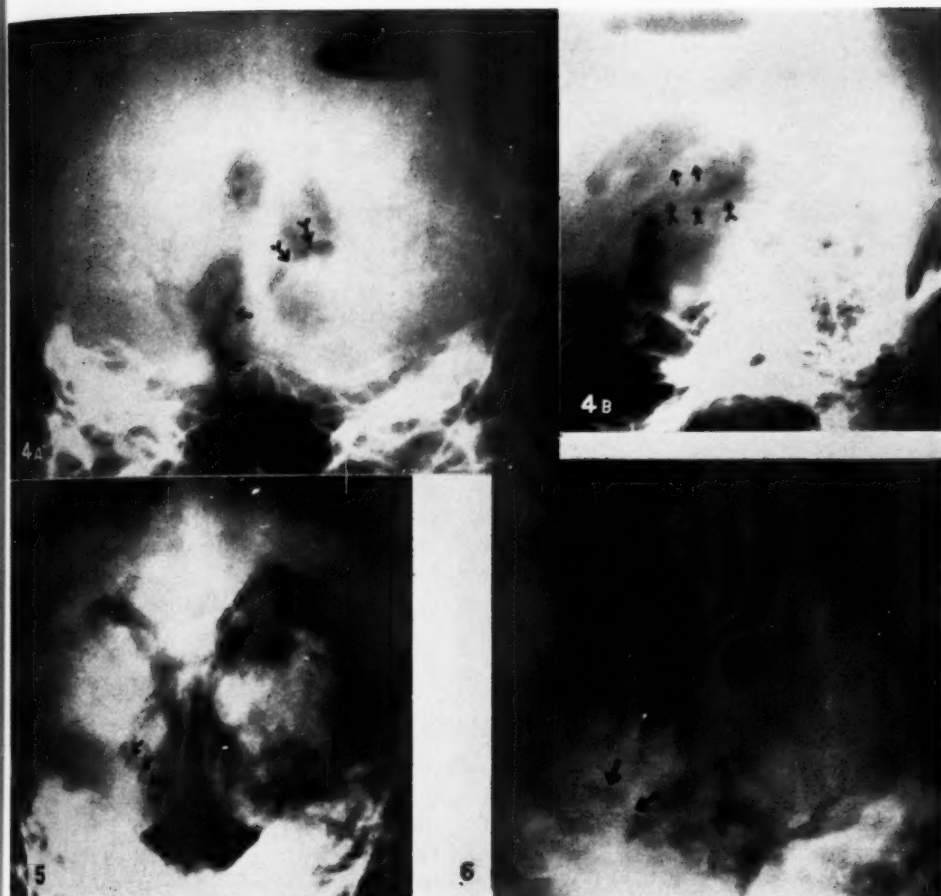


Fig. 4. Acoustic neuroma in a 64-year-old male. A. Frontal projection. The vallicula and interpeduncular cistern ( $\rightarrow$ ) are displaced to the right, forming a concave curve toward the tumor. Subarachnoid air is present over the tumor ( $\bullet\rightarrow$ ).

B. Lateral projection. Subarachnoid air partially outlines the tumor ( $\bullet\rightarrow$ ). The posterior third ventricle and aqueduct are displaced upward ( $\rightarrow$ ).

Fig. 5. Acoustic neuroma in a 34-year-old female. The right cerebellopontine angle cistern ( $\rightarrow$ ) is displaced by the lesion.

Fig. 6. Prostatic metastasis in a 52-year-old male. Displaced right cerebellopontine angle cistern ( $\rightarrow$ ).

angle proposed by Sutton (11). These measurements, however, are sometimes unsuccessful in detecting early expanding processes, and evaluation of the form of the aqueduct and fourth ventricle will, in general, be more informative. Upward displacement of the posterior third ventricle occurs in cases of posterior-fossa lesions but is of little localizing value. The appearance of the normal ambient and cerebellopontine angle cisterns, as seen on the half-axial postero-anterior film,

is illustrated in Figure 3. The normal quadrigeminal plate cistern (Fig. 1, A), ambient wing, pontine and interpeduncular cisterns are best seen on lateral projections. Demonstration of the cisterns is extremely important in many posterior-fossa lesions, particularly in extracerebral and upper brain-stem tumors. In fact, a specific diagnosis of tumors in these locations can be made by encephalography, whereas neoplasms of the cerebellum and fourth ventricle may obstruct the foramen of

Magendie sufficiently often that ventriculography is required for their complete demonstration.

#### EXTRACEREBRAL, PONTINE, AND MIDBRAIN EXPANDING LESIONS

The tumor most frequently found in the cerebellopontine angle is the acoustic neurinoma. Most acoustic tumors will erode the internal auditory meatus, but the extent of the lesion cannot be predicted without encephalography. If sufficiently large, the mass will displace the aqueduct and fourth ventricle upward and backward to form an increased curve (4, 6). Displacement to the contralateral side also eventually occurs.

In Figure 4 a large left acoustic neurinoma in a 64-year-old male is outlined partially by subarachnoid air in both lateral and frontal views. The aqueduct and posterior third ventricle are markedly displaced upward, and the vallecule and interpeduncular cistern to the right, forming a concave curve toward the tumor. A smaller acoustic tumor demonstrated by encephalography in a 34-year-old female displaced the right cerebellopontine angle cistern but produced no change in the ventricular structures (Fig. 5). A cerebellopontine angle mass was seen in a 52-year-old male with signs of an expanding lesion. Encephalography revealed displacement of the right cerebellopontine angle cistern (Fig. 6), outlining a small mass without displacement of the ventricular system. The right acoustic meatus showed no abnormality, but a slight erosion of the tegmen tympani near the meatus was noted. Upon excision, the mass proved to be a metastasis from prostatic carcinoma.

Ventriculography alone in the last two cited cases probably would have yielded no useful information, and in the first case no definite statement about the extracerebral location and extent of the lesion could have been made solely from the ventriculographic findings. Meningiomas and cholesteatomas in the cerebellopontine angle may cause clinical

signs even when relatively small and although a few of these tumors produce skeletal erosions (1, 12), encephalography is essential for diagnosis in the majority. A normal crural cistern (Fig. 7) must be differentiated from a displaced cerebellopontine angle cistern when small tumors are suspected in this region.

The classic roentgen findings of a pontine glioma (10) were present in a 5-year-old female (Fig. 8). The compressed pontine cistern and the displaced fourth ventricle, aqueduct, and posterior third ventricle clearly outlined the tumor. Similar displacement of the ventricular structures may occur in clivus tumors, but filling of the pontine cistern leads to the correct diagnosis. A small clivus tumor in a 3-year-old boy (Fig. 9, A) was demonstrated on initial encephalography performed elsewhere. The small mass along the clivus outlined in the anterior pontine cistern caused minimal posterior displacement of the fourth ventricle and aqueduct. Three months later, at encephalography, a considerably larger mass was visualized obliterating the pontine cistern, with marked displacement of the fourth ventricle (Fig. 9, B). Surgery, and eventually autopsy, disclosed an undifferentiated extradural sarcoma with a large middle-fossa component.

A small space-occupying lesion in the region of the midbrain is illustrated in Figure 10. The upper aqueduct is displaced to the left, with slight tilting of the quadrigeminal plate to the same side (Fig. 10, A). Frontal projections also revealed a small mass in the posterior third ventricle (not illustrated). The patient, a 14-year-old girl with a history of sudden onset of headache, difficulty in upward gaze, and bloody spinal fluid, returned five months later for further evaluation. Encephalography then revealed that the aqueduct had returned to the midline but remained narrow and irregular (Fig. 10, B). The mass in the posterior third ventricle had disappeared. It was presumed that a small hemorrhage in the region of the quadrigeminal plate had

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Fig. 7. Normal crural cistern ( $\rightarrow$ ). The ambient and cerebellopontine angle cisterns are also filled with air ( $\bullet\rightarrow$ ). Note that the crural cistern crosses the ambient cistern.

Fig. 8. Pontine glioma in a 5-year-old female. Displacement of the fourth ventricle, aqueduct, and posterior third ventricle ( $\rightarrow$ ) and compression of the pontine cistern by the pontine mass ( $\bullet\rightarrow$ ).

Fig. 9. Extradural undifferentiated sarcoma in a 3-year-old male. A. First examination. There is a smooth-walled mass along the clivus outlined by air in the pontine cistern ( $\rightarrow$ ). The fourth ventricle is displaced slightly backward ( $\bullet\rightarrow$ ).

B. Second examination, three months later. The pontine cistern is obliterated and the mass extends into the interpeduncular cistern ( $\rightarrow$ ). The fourth ventricle was filled on other films and its posteriorly displaced position is indicated ( $\bullet\rightarrow$ ).

produced the initial encephalographic findings even though angiographic studies showed no vascular lesion. Vascular malformations of the midbrain may eventually result in an obstructive hydrocephalus from

recurrent bleeding and gliosis involving the aqueduct (9). Gliomas of the quadrigeminal plate are rare; they are recognized by filling of the aqueduct and the cistern over the quadrigeminal plate. The

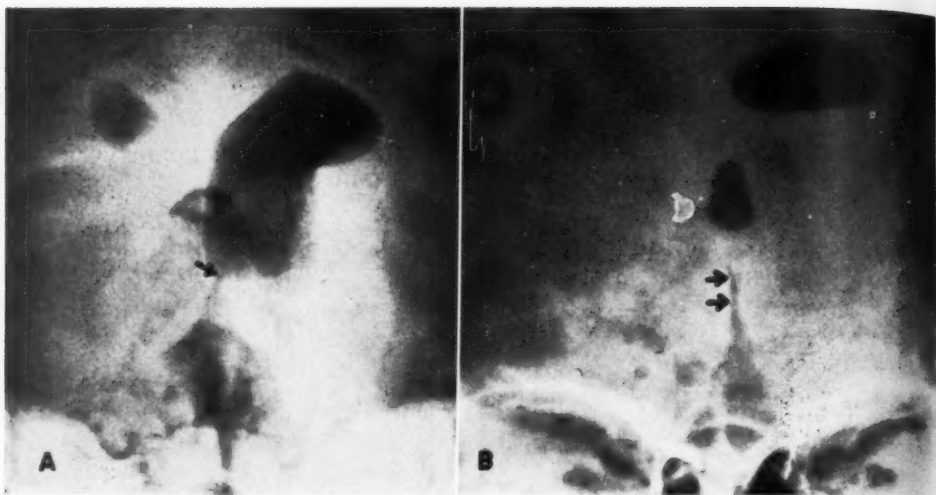


Fig. 10. Presumed hemorrhage in region of quadrigeminal plate, in a 14-year-old female.  
A. First examination. The aqueduct is displaced to the left ( $\rightarrow$ ), with tilting of the quadrigeminal plate to the left. Dilatation of the lateral ventricles is also seen.  
B. Second examination, five months later. The aqueduct is now midline but is narrow and irregular.

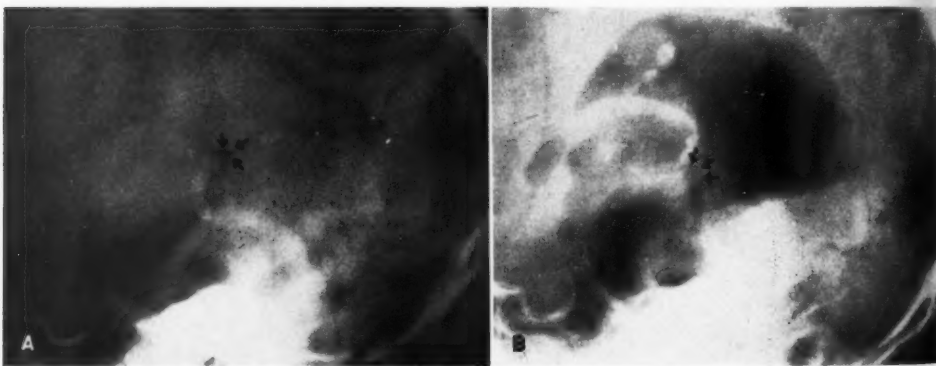


Fig. 11. Cerebellar hemangioblastoma in a 56-year-old female.  
A. Encephalography. A kink in the quadrigeminal plate is outlined by air in the cistern overlying this structure ( $\rightarrow$ ).  
B. Ventriculography. Aqueductal kink in same location ( $\rightarrow$ ). The lower aqueduct and fourth ventricle are displaced forward.

latter structure becomes thickened, and straightening and irregularity of the aqueduct occur (5).

Extracerebral tumors arising from the tentorial dura and cerebellar convexities theoretically would be better outlined by encephalography but, because of limited experience with such lesions, their differentiation from intracerebellar tumors will be discussed in respect to ventricular deformities alone.

#### CEREBELLAR AND FOURTH VENTRICLE TUMORS

Localization of tumors of the cerebellum and fourth ventricle depends primarily on certain characteristic deformities of the aqueduct and fourth ventricle (4, 8, 13). Some of these lesions cause only relative stenosis of the fourth ventricle and permit ventricular visualization by encephalography (4). This avoids the dangers of ventriculography (2), which

Fig. 12. Plate aqu. B. P. herniation. Fig. 13. and four pocketing. B. P.

however, a 56-year-old female with a cerebellar tumor. A. v.



Fig. 12. Cerebellar cyst with mural nodule, in a 6-year-old female. A. Lateral projection. Midquadrigenal plate aqueductal kink with forward displacement of dilated aqueduct and fourth ventricle ( $\rightarrow$ ). B. Postero-anterior projection. The aqueduct and fourth ventricle are displaced to the left ( $\leftrightarrow$ ), and upward herniation of the brain stem displaces the posterior third ventricle laterally.

Fig. 13. Medulloblastoma of fourth ventricle in a 15-year-old male. A. Lateral projection. The aqueduct and fourth ventricle are widely dilated. Note absence of pathologic aqueduct kink and presence of dorsal outpocketing at junction of the aqueduct and fourth ventricle. B. Postero-anterior projection. A large smooth-surfaced mass is partially outlined in the fourth ventricle.

however, as mentioned previously, is frequently necessary. Encephalography in a 56-year-old female with a right cerebellar hemisphere tumor showed nonfilling of the ventricular system but a small amount of cisternal air outlined a sharp kink in the quadrigeminal plate (Fig. 11, A). Ventriculography then revealed a

kink in the dilated aqueduct in the same location, with forward displacement of the lower aqueduct and fourth ventricle (Fig. 11, B). This latter kink is an exaggeration of the normal kink previously described. A cystic tumor of the right cerebellar hemisphere produced similar ventriculographic findings in a 6-year-old



girl (Fig. 12). A typical midquadrigenal plate aqueductal kink resulted from forward displacement of the lower aqueduct and fourth ventricle (Fig. 12, A). The tumor also displaced the aqueduct and fourth ventricle to the left, bulging into the latter structure (Fig. 12, B). Displacement of the posterior third ventricle laterally in this case was probably due to upward herniation of the brain stem.

Midline tumors of the upper cerebellar vermis usually cause a marked midquadrigenal plate aqueductal kink and frequently obstruct the junction of the aqueduct and fourth ventricle (5). These two structures remain in the midline on frontal projections, distinguishing such midline lesions from those in the cerebellar hemisphere or over the cerebellar convexities. Midline tentorial slit tumors, on the other hand, displace the entire quadrigenal plate anteriorly and inferiorly. The aqueductal kink then occurs at the junction of the posterior third ventricle and aqueduct instead of in the middle of the quadrigenal plate (4, 5). In addition to deforming the aqueduct and fourth ventricle, tumors beneath the lateral aspect of the tentorium often cause a bulging of the latter structure which displaces the homolateral trigone of the lateral ventricle (1, 12).

Processes expanding partially or entirely within the fourth ventricle are localized by demonstrating intraventricular filling defects. An example of a lesion primarily within the fourth ventricle was observed in a 15-year-old male (Fig. 13). A large, smooth-surfaced mass, partially outlined in the lower fourth ventricle, caused marked dilatation of the upper fourth ventricle and aqueduct. The aqueduct appeared funnel-shaped because of upward displacement of the inferior portion of the quadrigenal plate, and a dorsal outpocketing was evident at the junction of aqueduct and fourth ventricle (Fig. 13, A). This angular dorsal outpocketing represents a gross exaggeration of a slight bulge of the aqueduct at the junction of the superior medullary velum and quadrigenal

plate found in some normal persons (5).

As their size increases, intracerebral and extracerebral tumors in the region of the foramen magnum eventually produce dilatation of the entire ventricular system. The direction and magnitude of displacement of the fourth ventricle and aqueduct obviously depend on the site of origin and extent of the lesion. Small expanding lesions in this region may be difficult to detect by study of the aqueduct and fourth ventricle alone, since deformities of these structures may be minimal. Slight upward and lateral displacement of the fourth ventricle was noted in a 5-year-old female with a low midline cerebellar lesion extending inferiorly between the cerebellar tonsils (Fig. 14). Localization of the lesion was made possible by passage of a small amount of air (during ventriculography) into the subarachnoid space below the foramen magnum, thus outlining the lower pole of the tumor situated posterior to the cervical cord (Fig. 14, C). Differentiation of intracerebral or extracerebral tumors in this location from intramedullary expanding lesions in the high cervical cord is difficult unless the subarachnoid space below the foramen magnum is visualized.

#### AQUEDUCT STENOSIS AND POSTERIOR-FOSSA ARACHNOIDITIS

The differentiation of the non-neoplastic lesions—aqueduct stenosis and posterior fossa arachnoiditis—from tumors of the posterior fossa depends on complete demonstration of the aqueduct and fourth ventricle, frequently by a combination of encephalography and ventriculography. Ventriculography in benign aqueduct stenosis usually reveals a dilated short segment of the upper aqueduct with failure to fill the remaining aqueduct and fourth ventricle. Demonstration of the stenosis then depends on filling the fourth ventricle and lower aqueduct during encephalography. In cases of posterior fossa arachnoiditis, where the gliosis affects the foramina of Magendie and Luschka, encephalography usually results in nonfilling of

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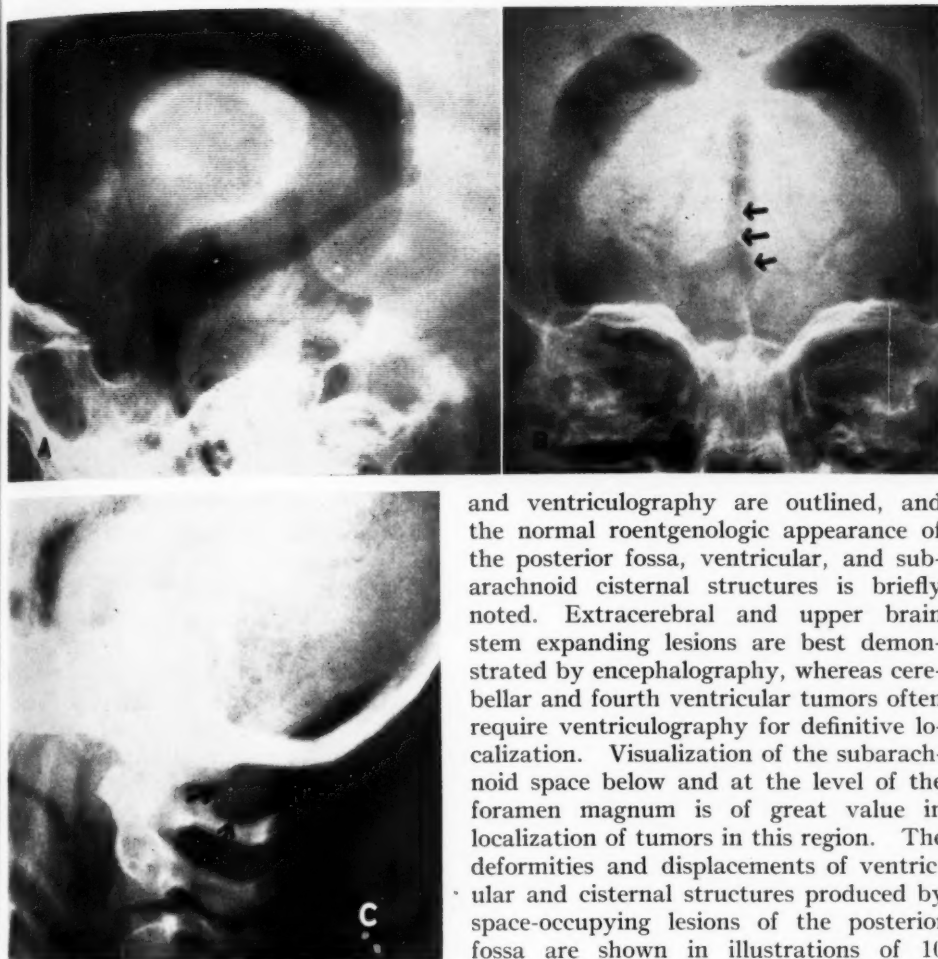


Fig. 14. Inferior midline cerebellar tumor in a 5-year-old female.

A. Lateral projection. Minimal upward displacement of the fourth ventricle.

B. Postero-anterior projection. Minimal displacement of the aqueduct and fourth ventricle to the right (→).

C. Lower pole of tumor outlined by subarachnoid air below the foramen magnum (→).

the ventricular system. The diagnosis is then obtained by ventriculography, which will show a dilated ventricular system, including the fourth ventricle, without structural displacement.

#### SUMMARY

Pneumographic evaluation of tumors of the posterior fossa is discussed. Some of the technical aspects of encephalography

and ventriculography are outlined, and the normal roentgenologic appearance of the posterior fossa, ventricular, and subarachnoid cisternal structures is briefly noted. Extracerebral and upper brain stem expanding lesions are best demonstrated by encephalography, whereas cerebellar and fourth ventricular tumors often require ventriculography for definitive localization. Visualization of the subarachnoid space below and at the level of the foramen magnum is of great value in localization of tumors in this region. The deformities and displacements of ventricular and cisternal structures produced by space-occupying lesions of the posterior fossa are shown in illustrations of 10 cases.

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St. Francis Hospital  
3630 Imperial Highway  
Lynwood, Calif.

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## SUMMARIO IN INTERLINGUA

## Tumor de Fossa Postero-Cranial

In le evaluation de tumores del fossa posterior, le diagnose final depende grandemente de studios pneumographic, i.e. encephalo- e ventriculographic. Le aspectos technic de iste methodos es discutite, e le normal roentgeno-apparentia del fossa posterior e del structuras ventricular e subarachnoide cisternal es describite. Un diagnose specific de multe tumores de fossa posterior—specialmente de tumores extracerebral e de tumores de pedunculo supero-cerebral—pote esser facite per encephalographia, durante que tumores del

cerebello e del quarte ventriculo obstrue le foramine de Magendie satis frequentemente pro requirer ventriculographia pro lor demonstration complete. Le visualisation del spatio subarachnoide infra le foramine magne e al nivello de illo es de grande valor in le localisation de tumores in iste region.

Le deformitates e displacements de structuras ventricular e cisternal producite per lesiones tridimensional del fossa posterior es monstrate in illustrationes ab 10 casos.



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# Ventricular Septal Defect and Severe Pulmonary Hypertension: Radiologic Considerations in Selection of Patients for Surgery<sup>1</sup>

CHARLES W. VICKERS, M.D., OWINGS W. KINCAID, M.D., JAMES W. DuSHANE, M.D., and JOHN W. KIRKLIN, M.D.

IN RECENT years surgical closure of defects in the ventricular septum has become a beneficial and relatively safe procedure. This increase in the scope of cardiac surgery demands specificity not only in establishing an accurate anatomic diagnosis but also in evaluating the associated hemodynamic alterations. One must be able to predict whether surgical closure of the anatomic defect will result in improvement or deterioration of the cardiac status.

There appears to be no unanimity of opinion among thoracic surgeons in regard to the criteria of operability for patients with ventricular septal defects and severe pulmonary hypertension. At the Mayo Clinic the decision as to operability has become increasingly dependent on the magnitude of the pulmonary artery flow, which is considered to be a reflection of the degree of resistance in the pulmonary vascular bed (3). It was the purpose of the study to be reported here to evaluate the role of conventional roentgen methods in estimating this flow in the presence of a ventricular septal defect.

## FUNCTIONAL PATHOLOGY OF VENTRICULAR SEPTAL DEFECT

A defect may occur in either the muscular or the membranous portion of the ventricular septum, but is found more commonly in the membranous portion which forms the superior part of the septum. Of more significance than the location of the defect is its size. In small defects (maladie de Roger), the normal differential pressure between the right and left ventricles is maintained and the magnitude of the arte-

rioventous shunt through the defect is not clinically significant. If the defect is large, however, the differential pressure between the ventricles is not maintained and the resultant arterioventous shunt may be 50 per cent or more of the left ventricular output. The consequent increase in the volume of blood and velocity of flow into the lesser circulation produces changes in the pulmonary vascular tree which may be recognized readily on the conventional postero-anterior roentgenogram of the thorax (2, 6, 7) (Figs. 1-4). These changes are usually manifested as an increase in the size of the main pulmonary artery and its branches, enlargement of both ventricles, and an associated hypoplastic aortic arch. Fluoroscopy shows vigorous pulsations of the central (hilar) branches of the pulmonary artery.

Ventricular septal defect is more frequently associated with pulmonary arterial hypertension than are most other cardiac anomalies. The hypertension may be due to two factors (4): (a) It may be the result of the increase in volume and velocity of blood entering the pulmonary circulation in the presence of normal pulmonary vascular resistance. Since the pulmonary resistance is normally about a fifth of that in the systemic vascular bed, the arterioventous shunt through any considerable defect is rather large and consequently the pulmonary artery flow is greatly increased. The pressure in the main pulmonary artery is elevated as a reflection of the left ventricular pressure. (b) Pulmonary hypertension may also result from increased pulmonary vascular resistance which obstructs the flow of blood through the smaller

<sup>1</sup> From the Mayo Clinic and Mayo Foundation (C. W. V., Assistant to the Staff; O. W. K., Section of Roentgenology; J. W. DuS., Section of Pediatrics; J. W. K., Section of Surgery). The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota. Accepted for publication in October 1959.

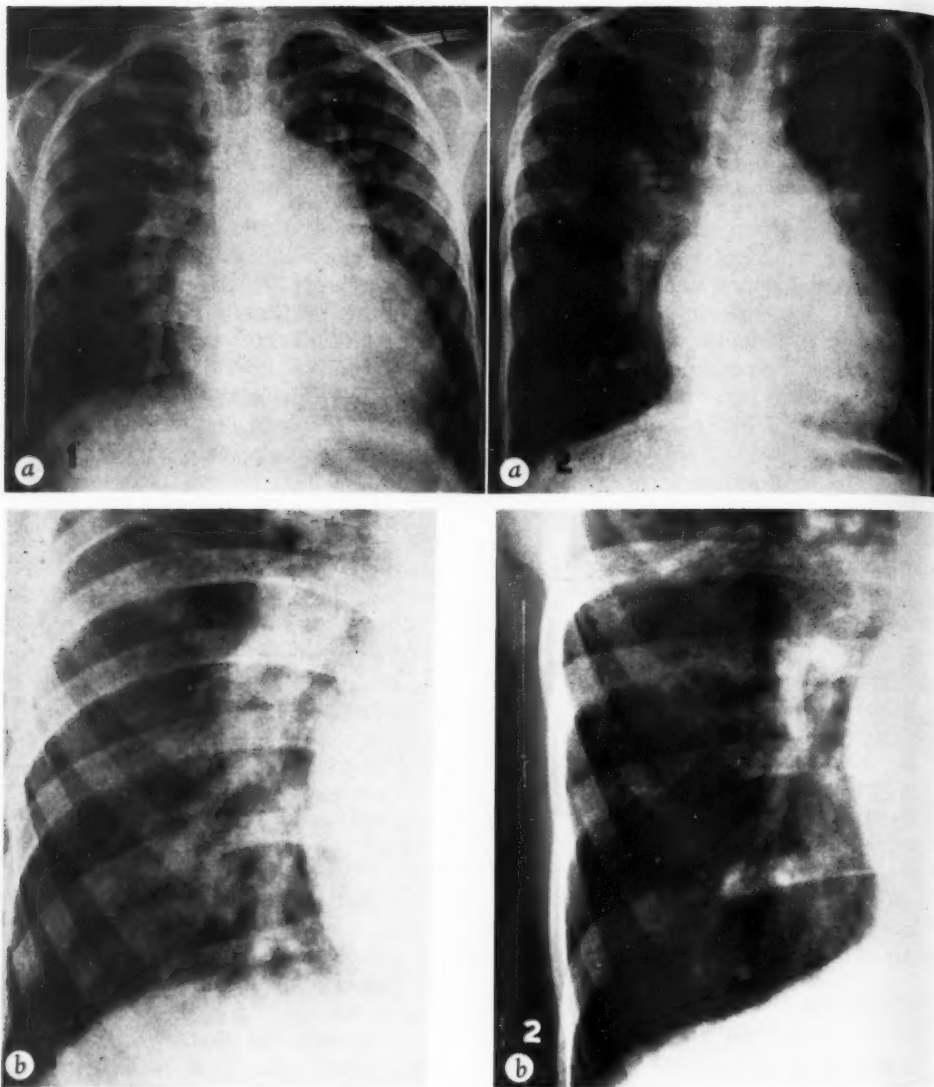


Fig. 1. *a.* Boy 8 years of age, clinically operable. Right ventricular pressure (systolic), 85 mm. of mercury. Large left-to-right shunt. Acyanotic. Surgical closure of the defect with good hemodynamic result. Postoperative right ventricular pressure (systolic), 30 mm. Hg. Considerable enlargement of main pulmonary artery and its central and peripheral branches. Cardiothoracic ratio, 0.60.

*b.* Magnified view of the right lower lung field to demonstrate better the normally tapering but greatly enlarged peripheral arteries.

Fig. 2. *a.* Nine-year-old girl, clinically operable. Main pulmonary artery pressure, 112 mm. Hg systolic and 74 mm. diastolic. Total pulmonary resistance, 580 dynes-second cm.<sup>-5</sup>. Left-to-right shunt, 41 per cent, right-to-left shunt, 10 per cent. Acyanotic. Defect surgically closed with good hemodynamic result. All pulmonary artery branches moderately enlarged. Cardiothoracic ratio, 0.58.

*b.* Magnified view of the right lower lung field to demonstrate better the enlargement of the peripheral arteries.

arteries and arterioles. The changes in the pulmonary vessels which are responsible for the increased resistance are pro-

gressive. As the resistance in the pulmonary vascular bed increases and more nearly approximates that in the systemic

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Fig. 3. Six-year-old girl, clinically operable. Right ventricular pressure (systolic), 60 mm. of mercury. Acyanotic. Defect surgically closed. Postoperative pressure in the right ventricle (systolic), 35 mm. Hg. Good hemodynamic result. Extreme enlargement of the main pulmonary artery and its central and peripheral branches. Cardiothoracic ratio, 0.58.

Fig. 4. Ten-year-old girl, clinically operable. Main pulmonary artery pressure, 83 mm. Hg systolic and 54 mm. diastolic. Total pulmonary resistance, 305 dynes-second-cm.<sup>-5</sup>. Acyanotic. A defect, 4 sq. cm., was closed surgically with a good hemodynamic result. Gross enlargement of the main pulmonary artery and its central and peripheral branches. Cardiothoracic ratio, 0.70.

vascular bed, the magnitude of the arteriovenous shunt and, therefore, the volume of pulmonary artery flow decrease. If the pulmonary resistance becomes greater than systemic resistance, the direction of the shunt is reversed and it becomes venoarterial or right-to-left (Eisenmenger complex). The pressure in the pulmonary trunk associated with greatly increased, normal, or decreased pulmonary flow may be equal to, but usually does not exceed, the systemic pressure.

A large arteriovenous shunt and increased pulmonary artery flow are associated with increased diastolic filling of the left ventricle. Because of this and the necessity of maintaining an adequate systemic circulation in the presence of a significant left-to-right shunt, the left ventricle enlarges. In this situation the right ventricle becomes dilated as a result of the increased volume of blood from the left-to-right shunt. If there is no great increase in pulmonary artery flow, however, the work load of the left ventricle remains unchanged and it is not enlarged.

Experience has shown that the presence or absence of increased pulmonary artery

flow may be predicted with considerable accuracy from the roentgenologic appearance of the heart and the pulmonary vessels. Increased pulmonary artery flow is manifested by enlargement of the main pulmonary artery and its central (hilar) and peripheral branches. Conversely, in those cases in which the main pulmonary artery and its right and left main branches are greatly enlarged but the peripheral branches are seen to be abruptly narrowed to a normal or a less-than-normal caliber, it may be assumed that there is no great increase in pulmonary artery flow but that the pressure in the pulmonary trunk is elevated as a result of increased peripheral pulmonary vascular resistance. In such cases it may be anticipated that the pressure in the main pulmonary artery will not be reduced after closure of the defect. The radiologic changes associated with a small, hemodynamically insignificant defect are negligible. The central and peripheral branches of the pulmonary artery are of normal caliber and the cardiac size and configuration are unaltered.

The size of the ventricles is also of

importance in evaluating pulmonary artery flow and operability, for reasons which have already been given. Experience gained at the operating table has shown that the presence or absence of ventricular enlargement can be determined with a fairly high degree of accuracy from the postero-anterior chest film.

In patients who have been operated on for correction of ventricular septal defect with a large arteriovenous shunt, it has been observed, at the time of operation, that the heart was enlarged in the transverse diameter. This enlargement was predominantly into the left hemithorax and was attributable to the enlarged left ventricle and the dilated right ventricle. Operation has been performed in a few patients with pulmonary arterial hypertension but little or no net left-to-right shunt and, therefore, no increase in pulmonary artery flow. In these cases the transverse diameter of the heart was not increased, although the right ventricle was always significantly hypertrophied, but not dilated. The presence or absence of ventricular enlargement in these cases can usually be determined roentgenologically with considerable accuracy.

We are of the opinion that, on the basis of these observations, it is often possible to predict the magnitude of pulmonary artery flow in cases of ventricular septal defect by evaluation of the cardiac silhouette and the relative sizes of the central and peripheral branches of the artery on the conventional postero-anterior roentgenogram.

#### METHODS AND MATERIALS

During the three-year period, 1955 through 1957, one group of surgeons at the Mayo Clinic performed operations for repair of ventricular septal defect on 91 patients in whom there was no evidence of complicating congenital or acquired malformations of the heart or great vessels, although increased pulmonary vascular resistance was present in many. During the same interval, 31 patients were seen in whom comprehensive clinical, physiologic,

and roentgen data indicated the presence of isolated ventricular septal defect complicated by increased pulmonary vascular resistance of such magnitude that the dominant shunt was right to left. This latter group was considered to be unsuitable for operation at the time of examination because of the suspicion that the pulmonary arterial hypertension might not be reduced by closure of the defect and that, therefore, a beneficial result would not be obtained.

In a few patients in each of these two groups criteria for or against surgical intervention were equivocal. The total number of such borderline cases was 12, in 4 of which operation was undertaken.

For the purpose of this study, the patients were divided into three categories, depending on the clinical evaluation of operability: 87 were considered operable, 12 borderline, and 23 inoperable. Patients with small ventricular septal defects who were not operated on because the physiologic changes were of insufficient magnitude to be considered significant were not included in this study.

The thoracic roentgenograms of all patients were evaluated independently, and the findings were correlated with the clinical and surgical appraisal as to operability. Since the ultimate decision on this point depends on the magnitude of the pulmonary artery flow, it is evident that the roentgenologic criteria by which the magnitude of that flow can be estimated are of first importance.

As was stated previously, it has been noted at the time of operation that enlargement of the ventricles, as a result of increased pulmonary artery flow in ventricular septal defect, produces an increase in the transverse diameter of the heart. In the presence of a normal or decreased pulmonary artery flow, there is little or no change in the size of the left ventricle, and the transverse cardiac diameter may be normal, even though the right ventricle is greatly hypertrophied. With this in mind, the cardiothoracic ratio was measured in each case.

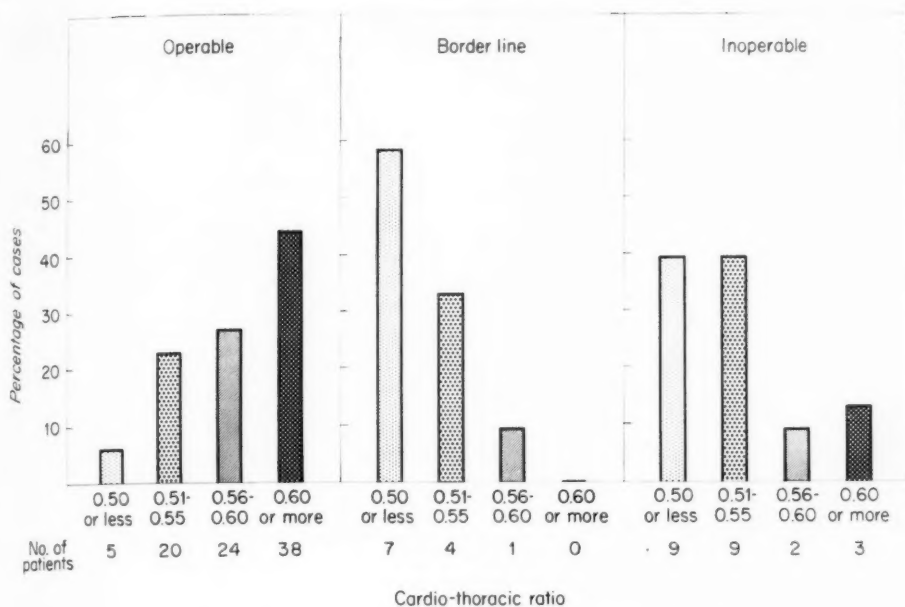


Fig. 5. Correlation of operability with the cardiothoracic ratio.

Increased pulmonary artery flow can also be estimated on the basis of size of the main pulmonary artery and its central and peripheral branches. In cases of high flow and low resistance the peripheral branches are enlarged in the same proportion as the central branches. Abrams (1), Keats and associates (5), and others have shown that the presence of pulmonary hypertension due to increased pulmonary resistance is manifested radiographically by an abrupt narrowing or tapering of the peripheral pulmonary arteries. In the present study, these changes were evaluated by estimating the relationship of the size of the central branches to the peripheral branches and tabulating deviations from the normal relationship. Actual measurement of the diameter of the vascular shadows was not attempted because of the difficulty encountered in duplicating exactly the site of measurement in the different patients and in correcting for the difference in patient size and age.

A review of the physiologic data made it evident that the pressure in the main pulmonary artery was rather high and

virtually equal to the systemic pressure in nearly all cases in all three categories. Almost all patients, then, had severe pulmonary hypertension. No attempt was made to correlate the pressure in the main pulmonary artery with the clinical or the roentgenographic evaluation of operability. In a few of the operable group, the pressure in the main pulmonary artery was only moderately elevated and these patients were found to have relatively small defects.

The total pulmonary resistance and the degree of left-to-right and right-to-left shunts, as determined at cardiac catheterization, bore a definite relationship to the clinical indications of operability. Correlation of catheterization findings with the roentgenologic criteria of operability would therefore seem unnecessary.

#### FINDINGS

**Operable Group:** In the 87 patients in whom the clinical evaluation indicated that surgical closure of the defect would produce a beneficial result, the roentgenologic manifestations were remarkably sim-

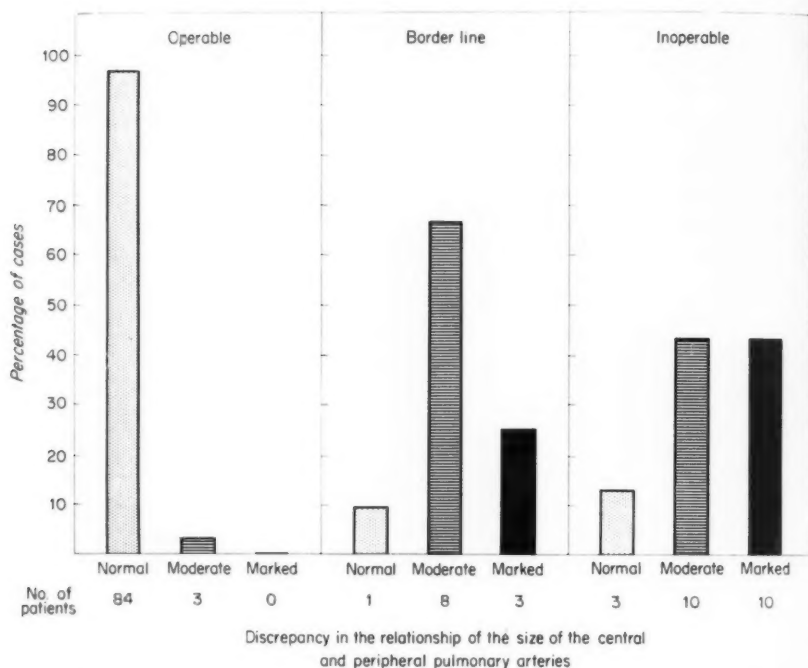


Fig. 6. Correlation of operability with roentgen evidence of the central and peripheral pulmonary arteries

ilar. The typical findings on the conventional postero-anterior chest film were an increase in the transverse diameter of the heart and gross enlargement of the main pulmonary artery and its central and peripheral branches (Figs. 1-4).

In 94 per cent of the 87 patients (82 patients) the cardiothoracic ratio was greater than 0.50 and in 44 per cent (38 patients) it was greater than 0.60 (Fig. 5). As mentioned previously, this increase in the transverse diameter of the heart is a manifestation of left and right ventricular enlargement. In 6 per cent of the 87 cases (5 patients) in which the cardiothoracic ratio was 0.50 or less, the defect was small and the resultant hemodynamic alterations were mild.

The relationship between the size of the main pulmonary artery and its central and peripheral branches was found to be normal in 97 per cent (84 patients) of this operable group (Fig. 6). In only 3 patients was there a moderate discrepancy between the size of the large elastic

arteries and the peripheral arteries. One of this number had a postoperative pressure in the right ventricle of 55 mm. of mercury and died of heart block on the fourth day after operation. A moderately severe degree of increased pulmonary vascular resistance may be assumed to have been present in this instance. The other 2 did well after operation without evidence of residual pulmonary hypertension.

It is significant that all patients in the operable group, with the single exception mentioned in the preceding paragraph, had definitely reduced pulmonary artery pressures postoperatively. Those in whom a complete closure of the defect was possible and who survived beyond the postoperative period were virtually free of organic cardiac symptoms.

**Borderline Group:** The clinical evaluation of operability was equivocal in 12 patients, 4 of whom underwent operation. In this group, the roentgenologic evaluation indicated, for the most part, the

Fig. 7. Main pulmonary artery and peripheral branches. 2,420 cent; years, and the Cardiac

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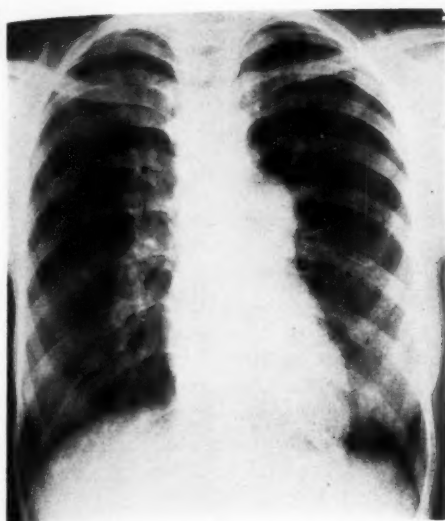


Fig. 7. Girl 13 years of age, clinically inoperable. Main pulmonary artery pressure, 126 mm. Hg systolic and 75 mm. diastolic. Total pulmonary resistance, 2,420 dynes-second-cm.<sup>-5</sup>. Left-to-right shunt, 9 per cent; right-to-left shunt, 24 per cent. Cyanotic for years. The central branches are moderately enlarged and the peripheral branches are of normal caliber. Cardiothoracic ratio, 0.41.

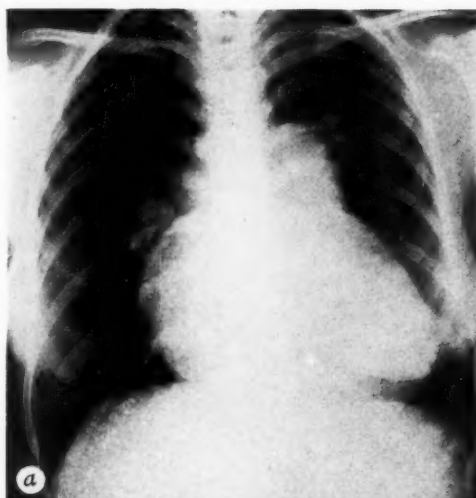


Fig. 8. *a.* Woman 25 years of age, clinically inoperable. Main pulmonary artery pressure, 124 mm. Hg systolic and 66 mm. diastolic. Total pulmonary resistance, 2,463 dynes-second cm.<sup>-5</sup>. History of progressive cyanosis for four to five months. The main pulmonary artery and its central and peripheral branches are greatly enlarged and the peripheral branches are normal. Cardiothoracic ratio, 0.65. Since the history of right-to-left shunt is of relatively short duration, it may be assumed that the left ventricle has not had sufficient time to become normal in size.

*b.* Magnified view of the right lung field to demonstrate better the abrupt narrowing of the peripheral arteries.

presence of increased pulmonary vascular resistance.

The cardiothoracic ratio was 0.50 or less in 58 per cent of the 12 patients (7 patients) and was 0.55 or less in 91 per cent (11 patients) (Fig. 5). In only 1 case (9 per cent) did it exceed 0.55, and in this instance the heart was only moderately enlarged.

The ratio between the size of the central branch and that of the peripheral branches of the pulmonary artery was abnormally increased in 91 per cent (11 patients) of this group (Fig. 6). In 66 per cent (8 patients) the discrepancy in size was moderate and in 25 per cent (3 patients) it was large. In only 1 patient (9 per cent) was the relationship normal.

**Inoperable Group:** In all 23 patients in the inoperable group, there was definite clinical evidence of inoperability in the form of cyanosis or a history of cyanosis on exertion, electrocardiographic evidence of right ventricular hypertrophy with absence of increased workload on the left ventricle, or the finding at cardiac catheterization of





Fig. 9. Eleven-year-old girl with main pulmonary artery pressure of 102 mm. Hg systolic and 44 mm. diastolic. Total pulmonary resistance, 937 dynes-second-cm.<sup>-5</sup>. Defect surgically closed. Postoperative pressure in main pulmonary artery, 96 mm. systolic and 50 mm. diastolic. Patient is still living but has persistent pulmonary hypertension. The main pulmonary artery is moderately enlarged and the peripheral artery branches are of normal caliber. Cardiothoracic ratio, 0.49.

a bidirectional shunt with a predominant right-to-left shunt at the ventricular level.

The cardiothoracic ratio was normal or only slightly increased in 78 per cent (18 patients) of this group (Fig. 5). It was moderately increased in 9 per cent (2 patients), and in 13 per cent (3 patients) was greatly increased. In these 5 patients in whom the transverse diameter of the heart was significantly increased in spite of elevated pulmonary resistance, it is possible that the resistance in the pulmonary vascular bed was of fairly recent origin and that enough time had not yet elapsed for the left ventricle to become normal in size. It is possible also, although there was no clinical evidence to indicate it, that the diagnosis was inaccurate (Fig. 7). It is of interest that in a few patients in whom serial roentgenograms of the thorax were available, the transverse diameter of the heart could be seen to decrease progressively as the magnitude of the left-to-right shunt was reduced.

The ratio of the size of the central pulmonary artery to that of the peripheral branches was increased in 87 per cent (20 patients) of the inoperable group (Fig. 6). The discrepancy was moderate in 43.5 per cent (10 patients) and large in 43.5 per cent (10 patients). In 3 cases (13 per cent) the relationship was normal. In 2 of these 3 the transverse diameter of the heart was normal or only slightly above normal, and the combination of findings suggested the erroneous conclusion that the defect was small. In the third patient the transverse diameter of the heart was greatly increased and roentgenographically there were no signs to suggest inoperability. Examples of inoperable cases are shown in Figures 7-11.

#### COMMENT

It is apparent from the results of this study that much corroborative information may be contributed by the roentgenologist in establishing the presence or absence of resistance-type pulmonary hypertension and, therefore, operability in cases of known ventricular septal defect.

The roentgen criteria by which one may establish the presence of pulmonary hypertension which cannot be expected to be reduced by closure of the defect are (a) a normal or near-normal cardiothoracic ratio due to absence of left ventricular enlargement and (b) a discrepancy between the sizes of the central and peripheral branches of the pulmonary artery. It is evident that the transverse diameter of the heart, as estimated by the cardiothoracic ratio, is increased significantly in most patients in whom the left-to-right shunt is large. As was previously stated, this increase in the transverse dimension of the heart is a reflection of biventricular enlargement. In many patients having a high pulmonary vascular resistance and a right-to-left shunt, the heart is normal in size or only slightly enlarged, since the left ventricle is not usually enlarged under these conditions.

The central branches of the pulmonary arteries bear a normal relationship to the

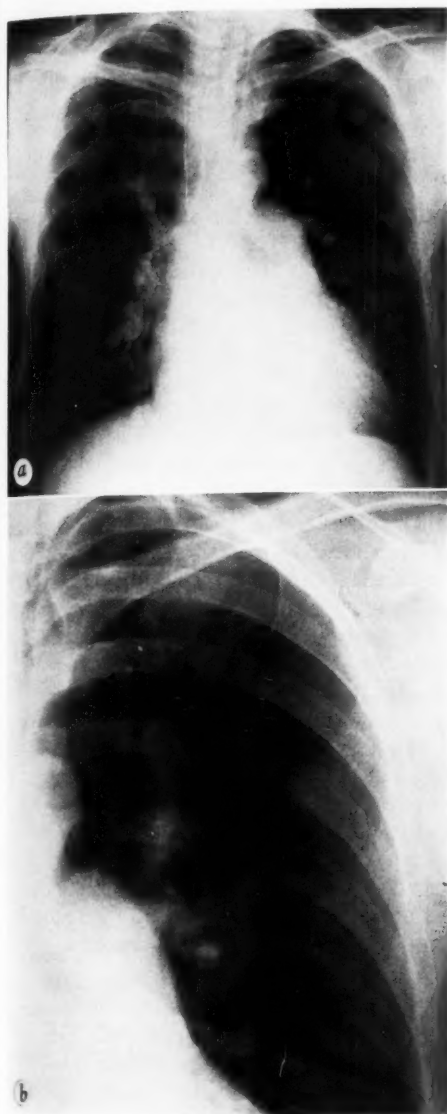


Fig. 10. a. Man 43 years of age, clinically inoperable. Pressure in main pulmonary artery, 110 mm. Hg systolic and 52 mm. diastolic. Total pulmonary resistance, 2,343 dynes second-cm.<sup>-5</sup>. Left-to-right shunt, 14 per cent; right-to-left shunt, 50 per cent. Cyanotic for years. The main pulmonary artery and its central branches are moderately enlarged; the peripheral branches are normal. Cardiothoracic ratio, 0.55.

b. Magnified view of the left upper lung field to demonstrate better the abrupt narrowing of the peripheral pulmonary artery branches.

peripheral branches in the presence of a large left-to-right shunt. All branches are grossly enlarged but there is no discrep-

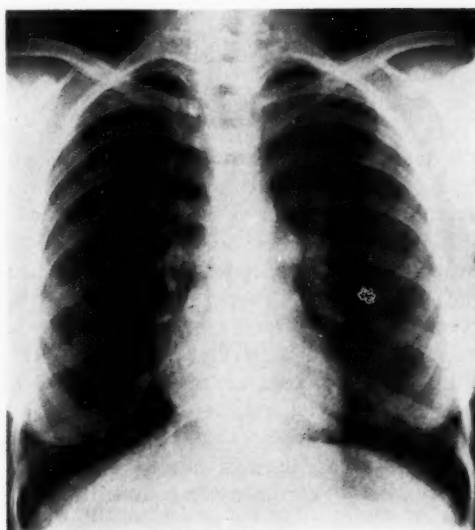


Fig. 11. Fourteen-year-old girl, clinically inoperable. Pressure in main pulmonary artery, 110 mm. Hg systolic and 60 mm. diastolic. Bidirectional shunt. Cyanotic for years. Moderate enlargement of the main pulmonary artery and its central branches; normal peripheral branches. Cardiothoracic ratio, 0.44.

ancy in the relative size. In the presence of severe peripheral pulmonary vascular resistance, the main pulmonary artery and its central branches are rather large and the tertiary or peripheral branches may be seen to narrow abruptly to a normal or even smaller-than-normal caliber.

It appears that these roentgenologic criteria are slightly more reliable in patients with a left-to-right shunt and in whom the peripheral pulmonary vascular resistance is normal. In these patients, an excellent hemodynamic result was invariably obtained from closure of the defect, and the similarity in the appearance of the roentgenograms of the thorax was remarkable.

In the 23 patients who were considered grossly inoperable from a clinical standpoint and in 4 who had persistent pulmonary hypertension after surgical closure of the defect, the roentgen criteria were slightly less constant. Of these 27 patients, 74 per cent (20 patients) had both a normal or near-normal transverse heart diameter and a discrepancy in size between the central and peripheral branches

of the pulmonary artery. In 15 per cent (4 patients), however, although there was the expected discrepancy in the size of the branches of the pulmonary artery, there was a moderate-to-large increase in the transverse measurement of the heart. In 7 per cent (2 patients) the heart size was normal or near normal, as was the relationship between the central and the peripheral branches of the pulmonary artery. In 1 patient in this inoperable group, the presence of an increased cardiothoracic ratio and a normal relationship between the size of the central and the peripheral branches of the pulmonary arteries indicated erroneously that the peripheral pulmonary vascular resistance was normal.

Obviously there are some limitations to the application of these roentgen criteria of operability in patients with ventricular septal defect. It has been emphasized repeatedly in the recent literature that the specific diagnosis of ventricular septal defect cannot be made by conventional roentgen means with any degree of certainty. It is necessary, therefore, that the diagnosis of ventricular septal defect be firmly established and that the coexistence of other cardiac malformations be excluded by clinical methods or by cardiac catheterization, or both, before these criteria are applied. Increased resistance in the pulmonary artery may be a complicating factor in other congenital lesions of the heart such as atrial septal defect, patent ductus arteriosus, anomalous pulmonary venous connection, and persistent common atrioventricular canal. The pulmonary vascular changes associated with these conditions are not unlike those in ventricular septal defect. Since the hemodynamic alterations and the associated anatomic changes differ so greatly in these various types of congenital heart disease, the criterion relating to the transverse cardiac diameter is not applicable in predicting their operability.

In reviewing the roentgenograms of the patients comprising this study, it was noted that evaluation of ventricular enlargement and of the pulmonary vessels

was extremely difficult in patients less than two years of age. It would seem, therefore, that these criteria of operability are of little practical value in this age group.

There is, at least in theory, another roentgen sign of increased peripheral pulmonary vascular resistance. Since there is a relatively small pulmonary artery flow in the presence of increased peripheral pulmonary vascular resistance, it seems reasonable to assume that, if the pulmonary valve is competent, there should be normal or, perhaps, subnormal pulsations in the central branches of the pulmonary artery. The reverse of this is true and is well documented (2, 5, 7), in patients with normal pulmonary resistance and a large left-to-right shunt through a ventricular septal defect. In such instances the central branches of the pulmonary artery are seen to pulsate vigorously ("hilar dance"). It was not possible to evaluate this sign adequately in the present study, since only a few of the patients had been examined fluoroscopically. It is of interest, however, that among 6 patients with excellent surgical results who were examined fluoroscopically, 5 were described as having exaggerated hilar pulsations. On the other hand, of 5 clinically inoperable patients in whom fluoroscopy was done, 4 were considered to have normal hilar pulsations.

#### SUMMARY

A brief summary of the anatomic and functional pathology of ventricular septal defect has been presented, with special emphasis on the manner in which some alterations are manifested roentgenologically. Determination of the magnitude of the pulmonary artery flow, which is a reflection of the peripheral pulmonary vascular resistance in the presence of a large defect, is the most significant point in the evaluation of patients with ventricular septal defect and in the selection of those who may benefit from surgical closure of the defect. Roentgen criteria of operability and inoperability have been

evaluated. The results of this study show that the presence or absence of increased peripheral pulmonary vascular resistance may be predicted in a high percentage of patients on the basis of the roentgen findings.

The decision as to operability in the individual patient with known ventricular septal defect is frequently difficult to make. While it is obvious that it must be based primarily on clinical aspects, the prediction of surgical success or failure can often be made on the roentgen findings. Roentgenology, then, may assume its place with cardiac catheterization and electrocardiography as a valuable aid to the cardiologist and surgeon on whose shoulders the final decision as to operability must rest.

Mayo Clinic  
Rochester, Minn.

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## SUMMARIO IN INTERLINGUA

**Defecto Ventriculo-Septal e Sever Hypertension Pulmonar: Considerationes Radiologic in le Selection de Patientes pro le Tractamento Chirurgic**

Es monstrate que il es frequentemente possibile predicar le magnitudine del fluxo pulmoararterial per le evaluation del silhouette cardiac e del dimensiones relative del brancas central e peripheric del arteria in le roentgenogramma postero-anterior routinari.

Esseva studiate tres grupos de patientes con significative defectos ventricular: 87 casos considerate como operabile super le base de criterios clinic, 12 casos liminal, e 23 casos considerate como imoperabile.

In le gruppo clinicamente considerate como operabile—i.e. le gruppo de patientes in qui il esseva justificate expectar que le clausion chirurgic del defecto producerea un effecto benefic—le constatactiones roentgenographic esseva typicamente augmento del diametro transverse del corde e allargamento grossier del major arteria pulmonar e de su brancas central e peripheric. In le casos liminal, le evaluation roentgenoscopic indicava in le majoritate del subjectos un aug-

mento del resistentia pulmono-vascular. In le majoritate de iste casos, le proportion cardio-thoracic esseva infra 0,55, e le proportion inter le dimensiones del brancas central e illos del brancas peripheric del arteria pulmonar esseva anormalmente augmentate. In le non-operabile gruppo, le criterios roentgenoscopic esseva levemente minus constante. In circa tres quartos del patientes le proportion cardio-thoracic esseva normal o quasi normal, e in le majoritate del casos le proportion inter le dimensiones del central arteria pulmonar e del brancas peripheric de illo esseva augmentate.

Es concludite que le roentgenologia pote prender su placia con le catheterismo cardiac e con le electrocardiographia como un utile auxilio pro le cardiologo e le chirurgico qui debe, ultimemente acceptar le responsabilitate del decision con respecto al operabilitate del casos de patientes qui suffre cognoscitementemente de defectos del septo ventricular.



# Angiography of the Internal Carotid with Use of the Catheter Technic<sup>1</sup>

P. ELFVIN, M.D.

SINCE SELDINGER in 1953 introduced his technic of inserting a catheter percutaneously, this method, either in its original or modified form, has been widely used for the examination of various vascular areas. Cerebral angiography, however, is still performed mainly with direct injections of contrast material through the puncture needle, according to the procedure described by Lindgren (1947). The frequency of complications with this method has gradually decreased as technic has improved and better and less toxic contrast media have become available. There are still reports, however, of serious, sometimes lethal, complications. Inadvertent intramural contrast injection has been described by several writers, including Liverud (1958), who in one year had 3 deaths due to occluding dissecting aneurysms resulting from this accident. Saltzman (1959) reported 101 extravasal injections in a series of 1,020 cerebral angiographic studies. The number of clinical complications is not given. Replacement of the sharp puncture needle by a soft catheter should eliminate the risk of complications of this type. Another disadvantage of the needle technic is the rather low degree of selectivity. In Saltzman's series only 58.5 per cent were internal carotid angiographic studies, the other 41.5 per cent being classified as common carotid angiography. In addition, an unintentional injection into the external carotid was first made.

That the catheter method has not been more commonly employed for cerebral angiography is no doubt due mainly to warnings against its use. Lindbom (1957) found a high frequency of spasm in the arteries of the extremity during catheter angiography. He assumes that anatomical resemblance between various ves-

sels—in this case between the medium coarse muscular arteries of the extremities and the carotid artery—corresponds to a similarity in tendency to spasm and therefore warns against inserting a catheter into the carotid artery. Wickbom and Bartley (1957) arrived at a similar, although less categorical, conclusion after analyzing their arteriographic series on extremities. They mention 2 cases of complications among 20 carotid angiographic examinations with a catheter. At least one of these was believed to be due to arterial spasm.

## CLINICAL MATERIAL

The catheter technic was employed in the performance of 124 internal carotid angiographic studies on 104 patients—45 females and 59 males—at Mölndal's Hospital (Mölndal, Sweden) between August 1956 and January 1959. The 124 examinations demonstrated 20 cerebral tumors (including cerebral metastases) and 15 vascular disorders consisting in arterial and arteriovenous aneurysms, carotid thromboses, and subdural hematomas. In 89 cases the findings were normal.

## TECHNIC

Premedication with morphine-scopolamine and a sterile technic are employed. After palpation for a suitable puncture site, comparatively far down on the common carotid artery, generally about 2 cm. above the clavicle medial to the sternocleidomastoid muscle, the anesthetic is injected. This consists in a small cutaneous infiltration and periarterial introduction of 8 to 10 ml. of 1.0 per cent Xylocain around the common carotid and its branching.

The arterial puncture is then performed with a Seldinger cannula (P 160) with an internal cannula and mandrin. The tip is directed about 30° cranially from the

<sup>1</sup> From the Roentgenological Department of Mölndal's Hospital (Head: Dr. E. Selander), Mölndal, Sweden. Accepted for publication in September 1959.



vertical plane. The cannula is carefully guided down toward the vessel, while palpation of the pulse just above the puncture site is carried out with the left hand. When the tip rests against the arterial wall, the pulsation becomes diffuse and disappears on slight pressure of the cannula. After the vessel has been punctured and the internal cannula has been removed, one makes sure that the tip of the external cannula is in the vascular lumen. The angle between the artery and the cannula is then decreased as much as possible and the guide is inserted. The puncture should thus be made with the cannula in a comparatively vertical position, the insertion of the guide with the cannula being accomplished as horizontally as possible. This is to prevent the guide from emerging into any puncture hole which may have occurred in the posterior wall of the artery.

A metal guide of 40 cm. length with a flexible end is inserted for a distance of about 10 cm., counting from the puncture site in the skin. Its curvature permits the guide in most cases to be directed into the desired arterial branch. If inserted with the concavity of its curvature in a posterolateral direction, the guide will find its way into the internal carotid artery; if the concavity is in an anteromedial direction during insertion, the guide will run into the external carotid artery.

The passage of the guide must be performed with caution. It should slide into place easily and painlessly. If any resistance is encountered, no force must be used. If the resistance is on a level with the tip of the cannula—which can easily be checked by subtracting from the total length of the guide its measurement outside the cannula—the guide should be removed and the position of the cannula should be adjusted. If the resistance occurs above the tip of the cannula, the guide should be pulled back a little, the cannula removed, and the catheter inserted. The guide is then removed and preliminary arteriography of the throat vessels is performed.

After insertion of the catheter and removal of the guide, a small tap piece is

screwed to the adapter of the catheter. For a catheter we use a polyethylene tube (PE 160) 20 cm. long, which has been trimmed according to Seldinger's method. The position of the catheter is checked by rapid injection of physiological saline. When it is correctly placed in the internal carotid artery, a pallor is seen at the root of the patient's nose. This rapidly disappears and the patient complains of a cold feeling inside the head, back of the eyes. If the catheter lies in the external carotid artery the pallor appears over the cheek and the patient experiences an uncomfortable sensation in his jaws and teeth. If the wrong branch of the common carotid artery has been entered, adjustment can be made by sliding the catheter down into the main trunk and, after a suitable rearrangement of the head, directing it upward again. In 85 per cent of the cases in our series, the catheter could be placed in the internal carotid artery; otherwise contrast material, either in a larger amount or of greater concentration, was injected into the common carotid artery with no disadvantage. With the catheter in the internal carotid artery, injections of 6 to 8 ml. 45 per cent Urografin were made; with the catheter in the common carotid artery, the same amount of 60 per cent or 10 ml. of 45 per cent Urografin was administered.

While the catheter lies within the vessel, frequent small injections of physiological saline should be given, but aspiration must first be performed.

#### RESULTS

Out of 124 studies there was one slight complication of short duration, in a male, aged fifty-four, who four weeks prior to the examination suffered a subarachnoid hemorrhage. No abnormal neurological findings were noted immediately before the examination. Right- and left-sided carotid angiographic studies were performed without complications. A widening of the anterior ramus communicans half the size of a pea was observed and aneurysm was suspected. One week later

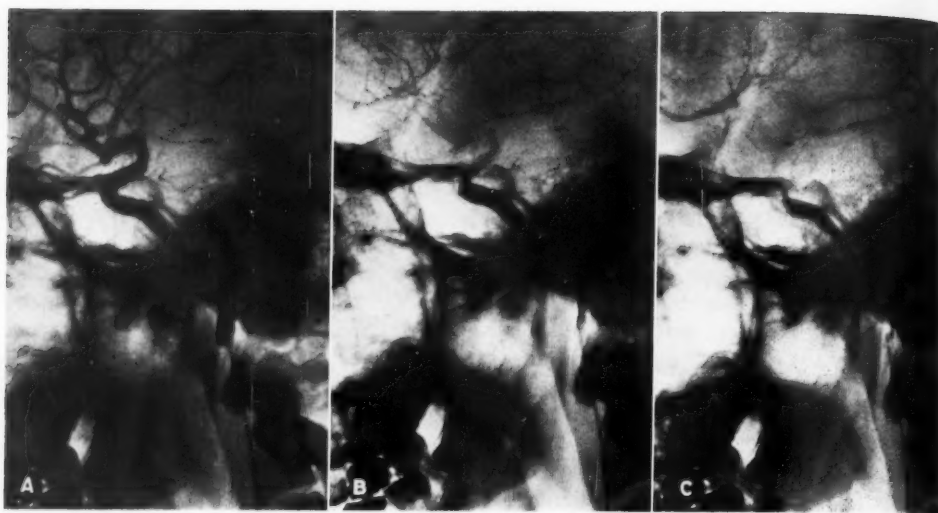


Fig. 1. Angiograms in one of two cases of arterial spasm. Note arterial contraction around the tip of the catheter, with residual contrast in the main trunk of the internal carotid, on views B and C, which were obtained about 1.5 to 2 and 3 to 4 seconds, respectively, after A. No clinical signs of complication.

left-sided angiography was again carried out. Two injections of 60 per cent contrast medium, one in the common and one in the internal carotid artery, were given to obtain lateral views. A further injection, also of 60 per cent contrast material, was then made into the internal carotid, with compression of the common carotid on the right side, for frontal views. About twenty minutes after the last injection, a slight, right-sided hemiparesis developed which had greatly improved after four hours and disappeared after three days. Nothing remarkable beside the aneurysm was found on the roentgenograms. There were no signs of arterial spasm and the circulation time seemed to be normal. This complication probably must be ascribed to the toxicity of the concentrated contrast agent accentuated by carotid compression. No other complications occurred.

In view of the tendency to local spasm, arteriographically demonstrated by several correspondents, following catheterization of medium-sized and fine muscular arteries of the extremities, our series of cases has been studied with reference to this point.

In 2 cases arterial spasm around the

catheter could be observed. In a fifteen-year-old boy with epilepsy, carotid angiography was performed in order to exclude cerebral tumor. The puncture and passage of the catheter were normal. With the catheter in the internal carotid, two injections of 6 and 10 ml. 60 per cent Urografin were given without any signs of arterial spasm. In order to examine further a suspected dislocation of the middle cerebral artery, an additional injection of 8 ml. 60 per cent contrast material was administered. A pronounced arterial contraction around the tip of the catheter, as well as severely retarded circulation (Fig. 1), could then be observed. No symptoms or findings deviating from the normal could be found after the examination, however.

Another patient, a male aged fifty-three, in poor general condition and suspected of having cerebral metastases, exhibited signs of increased intracranial pressure. The first injection, with the tip of the catheter in the common carotid artery, resulted, as in the first case, in contraction around the tip and retarded circulation. After the catheter had been placed further down in the common artery the examina-

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tion was completed without any signs of spasm. The patient showed no symptoms or findings of any complication after conclusion of the examination.

#### DISCUSSION

Lindbom in his series of 20 brachial arteriographic studies found arterial contraction around the catheter in all. In about half the cases the contraction was total and the circulation proceeded through collaterals. Wickbom and Bartley, in a series of 108 examinations of the extremities, reported arterial spasm in 39 per cent. In females less than thirty years of age the frequency of spasm was 75 per cent.

In our carotid angiographic studies only 2 cases were encountered with signs of arterial spasm, constituting 1.5 per cent of the entire series, with none in females. This astonishing difference in frequency of spasm must in our opinion be due to considerably less sensitivity to mechanical excitation in the carotid artery than in the arteries of the extremities, despite the anatomic resemblance. This assumption is supported by the known fact that the arteries of the central nervous system (as well as the coronary arteries) differ from the arteries of the extremities in their reaction to chemopharmacological stimulants.

The anesthetic probably is also of importance in avoiding arterial spasm. An extensive periarterial infiltration comparatively far down in the common carotid artery should give at least partial block of the sympathetic nervous system. (Horner's syndrome was found only once or twice.) Clinically a sympathetic block has been employed in arterial spasm of various origins, as in carotid spasm after periarterial injection with the needle method (Abbott, Gay, and Goodall; Kaplan and Walker, and others).

As previously mentioned, Wickbom and Bartley reported 2 complications in 20 catheter carotid angiographic studies. One of these, at least, was believed to depend on arterial spasm, but further details are not given. Liverud experienced no complication caused by spasm in 1,000

carotid angiographic examinations with the catheter. Nor were there any such complications in our 124 examinations. No further series examined by this technic has been published to our knowledge. The following conclusions seem therefore to be justified.

The experience gained thus far does not confirm the assumed danger of the method but, on the contrary, illustrates its advantages:

1. The risk involved in intramural and extravasal injections is eliminated.
2. The examination is easily borne by the patient.
3. Unlimited possibilities of special projections are afforded.
4. Examination of the common internal and external carotid arteries can be performed at the same examination without renewed puncture.
5. Automatic procedures with pressure syringe and film-changer enable the personnel to remain outside the examining room during the exposure.

The catheter method has one disadvantage: namely, it is more time-consuming than needle injection. The total time required for sterile arrangements and passing of the guide-catheter after the puncture is about five to ten minutes, but this, in our opinion, is of no importance as compared to the advantages gained.

#### SUMMARY

The catheter technic was employed in the performance of 124 internal carotid angiographic studies. The procedure is described and the observations are discussed with special reference to the risk of complications due to arterial spasm. In only 2 cases were minor arterial spasms, without sequelae, observed about the catheter tip. The method is recommended.

Lanslasarettet i Mölndal  
Mölndal, Sweden

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#### SUMMARIO IN INTERLINGUA

##### Angiographia del Carotide Interne, per Medio del Uso del Technica Catheteral

Le technica catheteral pro angiographia del carotide interne es describite. In 124 studios in 104 patientes effectuate al Hospital Mölndal (a Mölndal in Sveda), non plus que un sol e minor complication esseva incontrate, un leve hemiparese dextero-lateral que desapareva intra tres dies. Attention particular esseva prestate al occurrentia de spasmos arterial, proque altere autores ha reportate le tendentia a spasmo local post catheterismo arterial in le extremitates. In solmente 2 casos, un certe contraction esseva notate circum le puncta del catheter. Isto resultava in un retardo del circulation durante le injection, sed ni le un ni le altere del duo patientes manifestava ulle detegibile deviation ab le norma al conclusion del examine.

Le experientias colligite in le uso de iste methodo usque al tempore presente non

ha confirmate le periculo ascribite a illo; al contrario, illos demonstra su advantages.

(1) Le risco del occurrentia de injectiones intramural e extravasal es eliminate. (2) Le examine es facilmente supportate per le patientes. (3) Projectiones special deveni possibile sin ulle restriction. (4) Le examine del arterias carotic externe e interne commun pote esser effectuate in le mesme session, sin le necessitate de un secunde punction. (5) Dispositivos automatic con syringa de pression e excambiator de pellicula rende possibile que le personal remane foras del camera durante le exposition.

Le methodo ha possiblemente un disadvantage: Illo require cinque a dece minutas pro completar le mesuras de sterilisation e pro inserer le catheter-guida post le punction. Es opiniate que iste disadvantage es negligibile in comparison con le advantages del methodo.

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## Faulty Contrast Medium Injection in Percutaneous Ventricular Puncture<sup>1</sup>

BENJAMIN E. GREENBERG, M.D., and FREDERICK H. KNOX, M.D.

PERCUTANEOUS subxiphoid ventricular puncture, designated by Ponsdomenech and Núñez (6) as cardioangiography, has been shown to be a safe procedure for contrast delineation of the ventricular chambers of the heart and the outflow tracts, and for determining the competency of the mitral valve. It has been particularly useful in the diagnosis of conditions affecting the thoracic aorta and its branches and for clarification of the surgical anatomy with respect to operability. This report presents 6 instances of faulty contrast injection occurring in the course of a total of 41 percutaneous ventricular punctures. These cases along with those collected from the literature will be discussed as to incidence, radiographic features, and sequelae.

### LITERATURE

Ponsdomenech and Núñez carried out cardioangiography with manual injection of 70 per cent Diodrast in 56 instances in more than 30 patients. In 1 case the contrast medium was completely injected into the pericardial space without significant effect upon the patient. Smith *et al.* (7), using Diodrast and Hypaque, performed 33 injections in 32 patients with 1 instance of ventricular arrest, with recovery following cardiac massage. This accident was attributed to the injection of contrast medium directly into the left coronary artery. Lehman *et al.* (3) did ventricular punctures, a procedure which they termed cardiac ventriculography, 77 times in 60 patients. They used mechanical injection of 70 per cent Diodrast and rapid filming. Inadvertent intramyocardial injection occurred 8 times; in 1 patient with mitral valvular disease this mishap was followed by a complete heart block, which persisted. More recently Lehman and his

co-workers (4) in evaluating various methods of coronary artery opacification reported 230 ventricular punctures in 199 patients. Intramyocardial injection occurred in 5 cases, with 2 fatalities.

### METHOD

McCaughan and Pate (5) described in detail the method of ventricular puncture used at our hospital, with 31 injections in 29 patients. Briefly, it consists of rapid manual injection of 20 to 40 c.c. of 70 per cent Urokon with one or two needles. During the injection a Valsalva maneuver is maintained to raise the intrabronchial pressure and thus slow the rate of flow of the contrast medium (1). The patient is in the supine or right posterior oblique position. Serial exposures at two-second intervals are made immediately after completion of the injection for a total of 12. The Valsalva maneuver is discontinued at the end of or, in some instances, about midway in the exposure series. The results have been satisfactory both from a radiographic point of view and for diagnosis. Figure 1 shows films obtained by this procedure in a case of dissecting aneurysm of the aorta.

The present report covers a total of 41 injections in 38 patients up to April 1959 and includes the cases reported by McCaughan and Pate. Six instances of faulty contrast injection will be briefly documented.

### CASE REPORTS

CASE I (Fig. 2). *Pericardial Injection:* An adult male was investigated for an arteriovenous fistula of the left subclavian vessels following a stab wound. Elevation of the left diaphragm was attributed to phrenic nerve injury. The entire 25 c.c. of 70 per cent Urokon was injected into the pericardium with no untoward reaction. An electrocardiogram taken

<sup>1</sup>From the Radiology Service and Cardiology Section, Veterans Administration Hospital, Memphis 15, Tenn. (B. E. G., Chief, Radiology Service; F. H. K., Chief, Cardiology Section). Accepted for publication in October 1959.



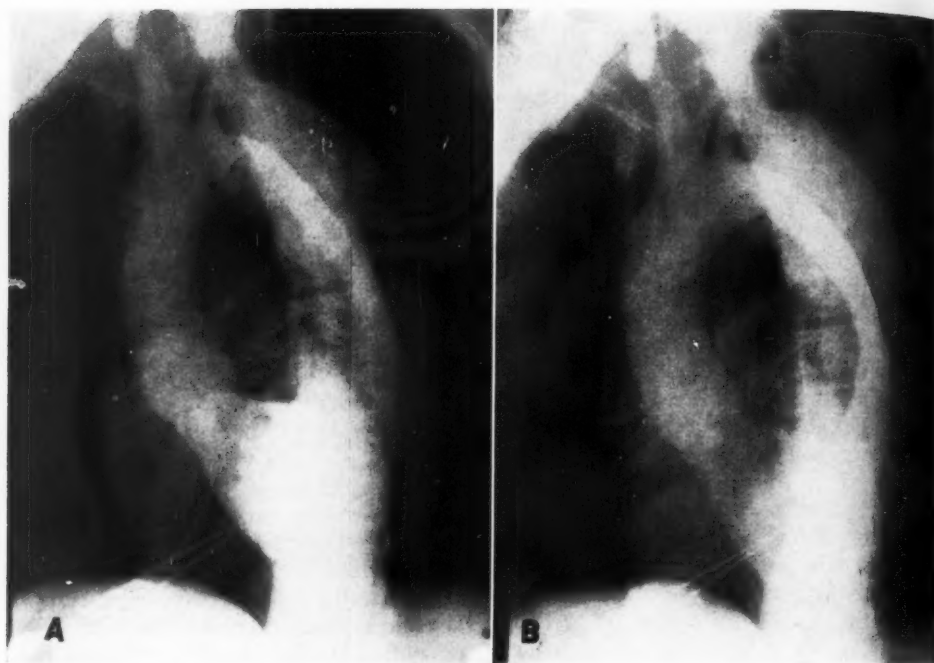


Fig. 1. Dissecting aneurysm of aorta. A. Contrast-filled narrowed lumen of the thoracic aorta with surrounding density free of contrast medium.

B. Later in the exposure series, contrast material enters the surrounding channel, demonstrating dissection. Surgery and autopsy confirmed dissection starting just distal to left subclavian artery.

shortly after the procedure was normal, and a radiograph obtained the following day showed no evidence of contrast medium.

**CASE II. (Fig. 3). Intramural Injection:** The patient seen as Case I had a second ventricular puncture a few months later, resulting in partial intramyocardial injection. A ventricular tachycardia lasted for a few minutes after the injection, with reversion to normal rhythm. A diagnostic cardioangiogram, however, demonstrated a false aneurysm of the left subclavian artery. This was confirmed at surgery. The simultaneous opacification of the coronary arteries and veins is of interest.

**CASE III (Fig. 4). Intramural Injection:** An adult male was studied for mitral regurgitation. Although contrast medium was partially injected into the wall of the ventricle and into the lumen, a diagnosis was obtained. A brief ventricular ectopic rhythm developed, with return of the pulse to normal in a few minutes. Electrocardiograms taken before and after the procedure were normal.

**CASE IV. Intramural Injection:** In an adult male with aneurysm of the aortic arch, contrast material was injected into the wall of the left ventricle with coronary vein visualization. Electrocardiography prior to the examination showed remote anterior



Fig. 2. Pericardial injection. Contrast medium in pericardium pooled about the great vessels and left cardiac border.

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Fig. 3. Intramural injection. Intramural and intraluminal contrast injection resulted in simultaneous opacification of the coronary arteries and veins. A false aneurysm of the left subclavian artery is demonstrated.

septal myocardial infarction. Following cardioangiography the findings were unchanged.

**CASE V. Intramural Injection:** An adult male with hypertension was examined for possible innominate artery aneurysm. Partial contrast injection into the ventricular wall resulted in coronary vein visualization. Ventricular tachycardia occurred, with a return to normal rhythm in a few minutes.



Fig. 4. Intramural injection. Contrast agent in wall and lumen of ventricle, with visualization of coronary veins.

**CASE VI (Fig. 5). Intramural and Pericardial Injection:** An adult male was investigated for possible aneurysm. Early in the exposure series there was evidence of intramural contrast medium and coronary vein opacification. Later, with discontinuance of the Valsalva maneuver and resumption of breathing, the contrast agent entered the pericardium. A ventricular tachycardia resulted, with return to normal rhythm in about six minutes. Only a tortuous aorta was demonstrated.

In the 6 instances of faulty injection of contrast medium encountered in this series, intramural injection occurred 4 times, pericardial injection once, and in 1 case there were concurrent intramural and pericardial injection of contrast medium.

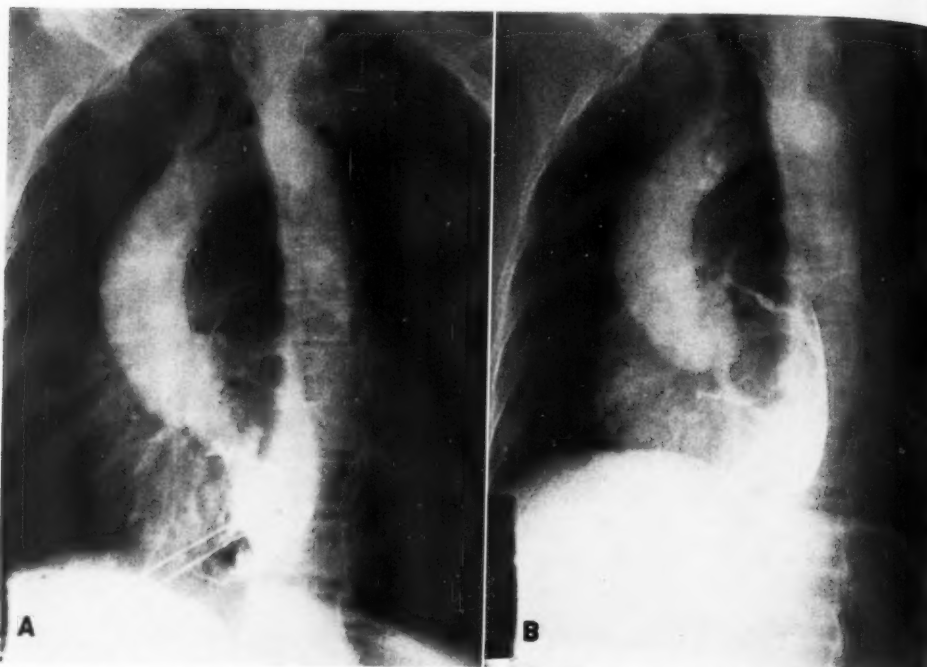


Fig. 5. Intramural and pericardial injection. A. Contrast material injected into ventricular wall, with coronary vein visualization, and also into the lumen, with a resulting diagnostic cardioangiogram. The left coronary artery is opacified.

B. Pericardial injection of contrast agent after discontinuance of Valsalva maneuver. Note elevated position of diaphragm.

#### DISCUSSION

A total of 42 instances of faulty contrast medium injection, in a total of 437 attempted or completed ventricular punctures, have been reported by various authors, including 6 described above. The data are summarized in Table I. If rapid-sequence multiple films are not used, evidence of intramural injection may be overlooked because of the radiographic similarity to the normal trabeculae of the ventricular contour in some projections. Venous opacification is unequivocal evidence of intramural injection of contrast substance. It is suspected that this complication is more frequent than the literature indicates. No serious immediate or delayed injury resulted from this complication in our cases, even in the presence of aortic aneurysm, hypertensive heart disease, and old myocardial infarction. Smith *et al.* (7) encountered a serious complication following inadvertent in-

jection of the contrast medium into the left coronary artery, but cardiac massage averted a fatality. Lehman *et al.* (4), with the largest reported series, had 2 fatalities as a consequence of intramyocardial contrast injection.

Pericardial injection of contrast medium appears to be innocuous, not even producing significant electrocardiographic changes.

Lehman *et al.* (3, 4) believe ventricular puncture to be associated with some hazard and list as contraindications atrial fibrillation with poorly controlled ventricular rate, paroxysmal atrial tachycardia, and atrial tachycardia resulting from atropine administration. Because ventricular tachycardia results from intramural injection a patient with this arrhythmia should be considered unsuitable for the procedure.

The risk of reaction to iodine-containing contrast media is of course also present.

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TABLE I: DATA ON 437 ATTEMPTED OR COMPLETED VENTRICULAR PUNCTURES REPORTED BY VARIOUS AUTHORS

Author	Total No. of Injections	No. of Patients	Faulty Injections	Intramural Injection	Pericardial Injection	Combined Intramural and Pericardial Injection
Ponsdomenech and Núñez (6)	56	30+	1		1	
Smith, Clegg, and Klassen (7)	33	32	1*			
Lehman, Musser, and Lykens (3)	77	60	8	7		2
Lehman, Boyer, and Winter (4)	230	199	26	5†		
Greenberg and Knox	41	38	6	4	1	1
TOTAL	437	359+	42	16	2	3

\* Left coronary injection.

† Including 2 fatalities.

regardless of whether or not the injection is made properly.

# SUMMARY

The radiographic features of 6 instances of inadvertent contrast injection in subxiphoid percutaneous ventricular puncture have been presented, with inclusion of intramural, pericardial, and combined faulty injections. A total of 42 such complications occurred in 437 injections carried out by various authors.

There were only 2 reported fatalities in spite of the presence of associated serious disease of the heart and great vessels.<sup>2</sup>

Since ventricular tachycardia of short duration results from intramural injection, the presence of this arrhythmia should be one of the contraindications to ventricular puncture, others being certain arrhythmias of atrial origin.

<sup>1</sup> In a paper appearing after completion of this study, a third fatality due to faulty injection was reported (Lehman, J. S.: Cardiac Ventriculography: Practical Considerations. *Progr. Cardiovas. Dis.* 2: 52-63, July 1959).

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Park Ave. and Getwell St.  
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# SUMMARIO IN INTERLINGUA

## Defectuositates del Injection de Substantia de Contrasto in Percutane Punction Ventricular

Subcutanee punction ventricular subxiphoidic—designate a vices como cardioangiographia o ventriculographia cardiac—es utile in le delineation contrastal del cameras ventricular e del vias de effluxo, in le determination del competentia del

valvula mitral, in le effectuation del diagnose de conditiones que affice le aorta thoracic e le brancas de illo, e in le clarification del anatomia chirurgic con respecto al question del operabilitate in le caso individual.

Le presente articulo se occupa de un total de 41 injectiones effectuate ante april 1959 in 38 patientes. Le serie include 6 casos de defectuositate del injection. Iste casos es describite in detalio. Le pertinente litteratura es revistate brevemente, e un total de 21 tal complicationes es tabulate ab series cooperante 437 injectiones individual. Casos mortal es relativamente rar. Le condi-

tiones que rende le methodo contra-indicate include fibrillation atrial con mal stabilisate frequentia ventricular, paroxysmic tachycardia atrial, e tachycardia resultante ab le administration de atropina. Viste que tachycardia ventricular resulta ab injection intramural, le patiente con iste typo de arrhythmia etiam debe esser considerate como non apte a esser studiate per iste methodo.



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## Microangiographic Study of the Vasa Vasorum of the Thoracic Aorta<sup>1</sup>

AYRES DE SOUSA, D.M., and LUIZ ALVARES, M.D.

THE PRESENT paper is concerned with the application of microradiography to the study of the vasa vasorum of the thoracic aorta. Relatively little attention has been given to these small vessels, though the work of Woodruff (1926), Winternitz *et al.* (1938), and Celestino da Costa (1945) may be mentioned.

The walls of the main arterial vessels consist of three layers. (a) The *intima* is formed by the endothelium, which is an element common to the whole vascular tree and the agent for the metabolic exchange between the blood and tissues. (b) The *media*, formed essentially by elastic tissue, is limited internally by the internal elastic membrane and externally by the external elastic membrane, which as a rule is less constant and less differentiated than the former. (c) The *adventitia* consists of connective tissue and elastic fibers. The nutrition of the arterial wall is provided by a network of small vessels, the vasa vasorum.

The observation that vessels less than 1 mm. in caliber had no vasa vasorum led Petroff (1922) and Anitschkow (1925) to demonstrate diffusion of plasma through the vessel wall. They injected dogs intravenously with trypan blue and found, on sacrificing the animal, that the aortic wall was tinged blue in its internal third, where there are no vascular structures. In animals that were allowed to live longer, the entire aortic wall was stained blue. Thus it was shown that substances in suspension in the blood could diffuse from the lumen of a vessel into its walls. This interstitial diffusion of the plasma is a relatively slow process and demonstration of its essential mechanism is difficult.

The vasa vasorum arise mainly from the collateral branches of the aorta, and only rarely from the aorta itself, the collater-

als involved being the coronary arteries, the intercostal arteries, and the lumbar arteries and other branches of the abdominal aorta. The vasa vasorum form two layers, one lying superficially on the adventitia and the other forming the main network in the adventitia. The system originating in any one collateral anastomoses with those of neighboring systems, producing a true perivascular "sleeve." The type of network in the thoracic aorta is slightly different from that in the abdominal aorta due to the fact that the intercostal arteries are situated posteriorly. This produces a richer network in the posterior aortic wall. In the abdominal aorta (which has major vessels arising anteriorly) the network is more uniform.

da Costa (1945) called attention to accentuations of the network at the level of the diaphragmatic hiatus, the celiac axis artery, and the bifurcation of the aorta. He thinks that these may have a functional significance in relation to the regulation of the circulation.

The vessels of the adventitia supply blood to the deep layers of the arterial wall. The depth to which they reach is, however, a matter of controversy. Winternitz (1938), and Woodruff (1926) are of the opinion that the vasa vasorum reach not only the media but also the intima, while Plotnikow (1884) maintained that they do not go beyond the outer third of the media, the intima and the inner two-thirds of the media being dependent on the interstitial circulation of the plasma. da Costa (1945) thought that in the majority of cases the arterial wall is irrigated by the vasa vasorum only in its outer layers, the inner ones being dependent upon diffusion of plasma. The degree and extent of irrigation by the vasa vasorum and the diffusion of plasma vary with the species and with

<sup>1</sup> From the X-Ray Department, Faculty of Medicine and Hospital Sta Maria, Lisbon, Portugal. Accepted for publication in November 1959.



Fig. 1. Typical sinuous pattern of the vessels of the adventitia.  $\times 40$

the individual. It has been shown, however, that there is no fundamental variation in the adventitial network of the aortas in man, dog, and the cat.

Because of special properties of permeability of the intima, the two systems of circulation—the vasa vasorum and plasma diffusion—are intimately linked to such an extent that the return circulation, which carries the catabolic products, is *via* the adventitial veins. Short (1940) states that even in the case of the vasa vasorum of the veins, the return circulation is directed toward the veins of the adventitia rather than to the lumen of the main vessel.

#### METHOD

The observations reported above have all been reached through the use of staining dyes, but the literature on the subject is rather sparse. We have used for the first time the technic of microangiography in the study of the vasa vasorum filled with contrast medium.

Trueta (1947) in Oxford studied the circulation of the kidney by microangiography. Bellman (1955) made extensive micrographic studies, particularly of the vascular system of the ovary. Braithwaite and Brockis (1951) and Brockis (1953) investigated the circulation of the extensor and flexor tendons and tendon grafts. Trueta and Harrison (1953) worked on the pathology of the hip joint, attempting to corre-

late it with the fine circulation of the head of the femur. Tirman *et al.* (1951) published their findings on microangiography of the mucosa of the esophagus, stomach, jejunum, ileum, ureter, and endocrine

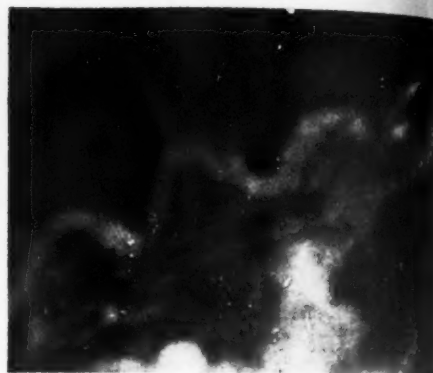


Fig. 2. Marked sinuosity of a vessel of the adventitia of the aortic arch in man.  $\times 80$

glands, while Meschan *et al.* (1955) dealt with the vascular pattern of the cerebral vessels. Collette (1953) studied the lymphatic vessels and the circulation of the eyeball, particularly the anastomoses of vessels of the optic nerve and retina. De Sousa and Cruz (1956, 1957) used the method for the investigation of the hepatic circulation, and Cruz *et al.* (1958) for the pulmonary circulation and the lymphatics of the lung. These investigators are at present engaged in research on the circulation of the skin and muscle.

#### TECHNIC

Microangiography is vasculography on a microscopic scale. The material for our work was obtained from the cadaver and the dog. The dogs were sacrificed by injection of chloroform. Once the thorax was open and the lungs and heart retracted out of the way, the aorta was carefully isolated and severed at the level of the diaphragmatic hiatus. All blood was removed by a thorough flushing with saline at  $38^{\circ}\text{C}$ ., after which the aorta was clamped at the level of the arch and the intercostal arteries were clamped 1 cm. distal to their origin. A barium suspension (50 per cent Micro-

Fig. 4. Th

paque in pressure, utes. T of its br running technic exactly 1 The s  $2 \times 2$  thickness each sec The va strated we cam fragmer duces ro ation o Fixatio cross se ple exp sufficien two fil wiched gether hours. The room a the sp thickn it ther tion) Sousa, into a



Fig. 3. "Ball-thread" pattern of the vasa vasorum.  $\times 45$

Fig. 4. The "knot" pattern, showing the loop and the branches running in opposite directions (dog).  $\times 75$

paque in water) was injected under manual pressure, which was kept up for five minutes. The aorta was then removed free of its branches, and the lumen washed in running water for half an hour. The technic of injection in the cadaver was exactly the same.

The specimen was cut in fragments of  $2 \times 2$  cm., and sections of the whole thickness of the wall were also obtained, each section measuring 250 to 300 micra. The vasa vasorum can thus be demonstrated in two planes. In our experience we came to realize that fixation of the fragments is inadvisable, since this produces retraction of the specimen and alteration of the architecture of the vessels. Fixation is recommended, however, for the cross sections. The fragments, after simple exposure to the air for half an hour, are sufficiently dry for mounting between two films of styrofoam and are then sandwiched between two glass slides held together by an elastic band for twenty-four hours.

The "sandwich" is taken to the dark room and, after removal of the glass slides, the specimen in its mount of styrofoam (the thickness of the styrofoam is 0.004 mm. and it therefore absorbs practically no radiation) is laid on a photographic plate (de Sousa, 1956) and the whole thing is put into a box whose opening is covered with

carbon paper fixed to it by an elastic band. The specimen is now ready to be x-rayed.

The x-ray unit has a low-voltage generator, the factors being 20 kvp and 20 ma for 1.5 seconds. The focus-film distance is 30 cm. Kodak D.158 developer in the proportion of one to two of water, at a temperature of  $20^{\circ}\text{C}$ ., is used. Fixation is done with standard preparations. Magnification is obtained by photographic means. In the study reported here magnifications up to  $200\times$  were used.

#### RESULTS

*Appearances:* One of the most striking findings was the sinuous appearance of most of the vasa vasorum (Fig. 1), except for the terminal ones, which were often straight. Regional variations were observed. At the level of the aortic arch, particularly on its superior surface, the sinuosity of the vessels was most marked (Fig. 2). Since this area undergoes the greatest expansion and withstands the greatest impact from the systolic wave, we believe that this characteristic morphology of the vasa vasorum permits their adaptation to the distention of the aortic wall without interference with its blood supply.

On the posterior wall of the aorta further characteristic patterns are found, with "thread-ball" formation, in which the caliber of the vessels is constant throughout

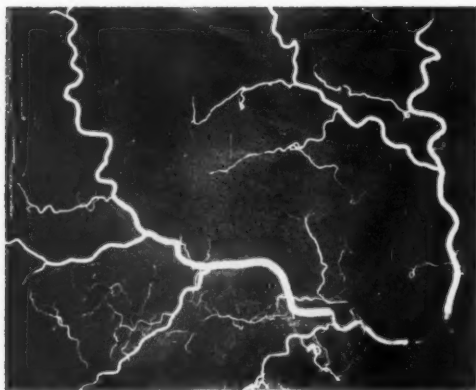


Fig. 5. Unilateral branching (dog).  $\times 45$

their complex course (Fig. 3). This architecture leads us to assume a damping mechanism. The collateral branches of the aorta and the branches from the latter to the adventitia take off at right angles and there appears to be between the main vessel and its adventitia a mechanism for damping the pressure. The sinuosity of the vasa vasorum is one more means of achieving this in the capillaries of the arterial wall.

The simplest mechanism of damping is the "knot," which is seen in the vessels that reach the adventitia coming from a collateral branch (Fig. 4). The resulting divisions run in opposite directions at an angle of  $180^\circ$ . Their bifurcations are mirror images of each other, with the same reduction of caliber.

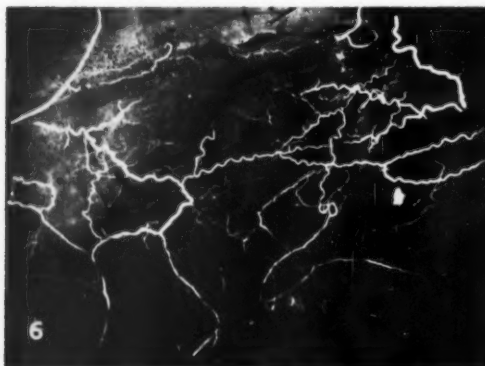


Fig. 6. Multiple anastomoses of the branches of the main vasa vasorum in the human aorta.  $\times 45$

Parallel to the normal division of the vessels there is a peculiar unilateral branching resembling a river, having confluent on its right or left bank only (Fig. 5).

**Anastomoses:** We have already mentioned the anastomoses in the adventitia between the vasa vasorum originating from adjacent aortic collateral branches. These anastomoses occur not only at the level of the precapillaries and capillaries but also at the level of the terminal branches (Fig. 6).

At the opening of the aortic collateral branches the markedly sinuous anastomoses have a coronal pattern (Fig. 7).

**Findings in Cross Sections:** The cross sections (Fig. 8) allow a study of the vasa vasorum in depth. The distribution of the vessels coming from the aortic collaterals and forming the adventitial network (Fig. 9) is of different types. In Type I the vessels run parallel to the surface and give off branches of smaller caliber, which enter either at a right angle or obliquely in to the depth of the adventitia. In Type II the vessels enter the adventitia at right angles, and their branches run parallel to the surface of the wall (Fig. 11). Type III is a "staircase" pattern. It is from the last step of the flight that there seems to arise the deeper network of the adventitial plexus described by Robertson (1929) (Fig. 12).

**Vascularization of the Media:** The vessels that run to the media are of very small

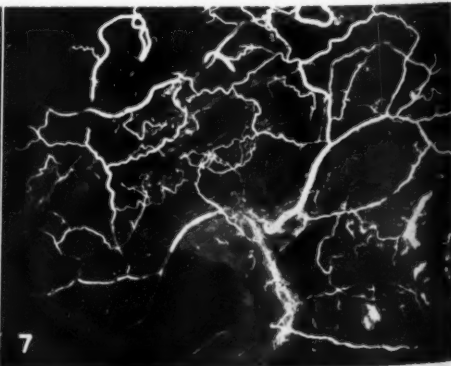


Fig. 7. "Coronal" pattern at the level of the origin of an intercostal artery (dog).  $\times 45$

caliber. Microangiography confirms the observation that they end for the most part at the outer third of the media.

Experimentally the study of the media is relatively simple because, after the injection of the contrast medium, it is easy to do an adventicectomy. The microgram will then show practically only the structures of the media and the vessels demonstrated are thin and short. The anastomoses are seldom long. The network formed is tighter and denser at the openings of the aortic collaterals.

#### SUMMARY

Microangiography is the method *par excellence* for the study of the vasa vasorum. Up until now this matter has been seriously neglected. The injection of dyes

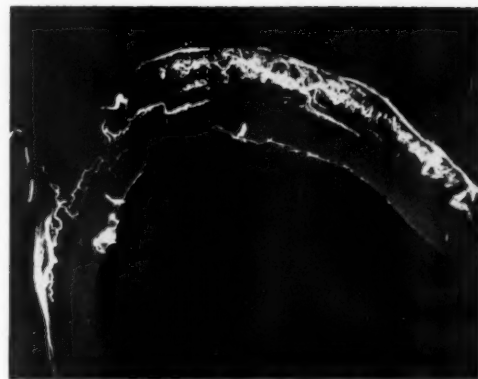


Fig. 8. Cross section of the human aorta.  $\times 4$

allows only the demonstration of the superficial vessels of larger caliber. Microangiography permits an easy and more readily

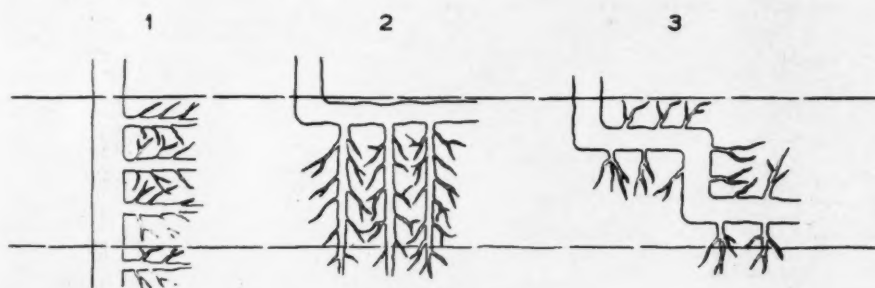


Fig. 9. The three patterns of cross-sectional branching of the vasa vasorum. See Figures 10, 11, and 12.

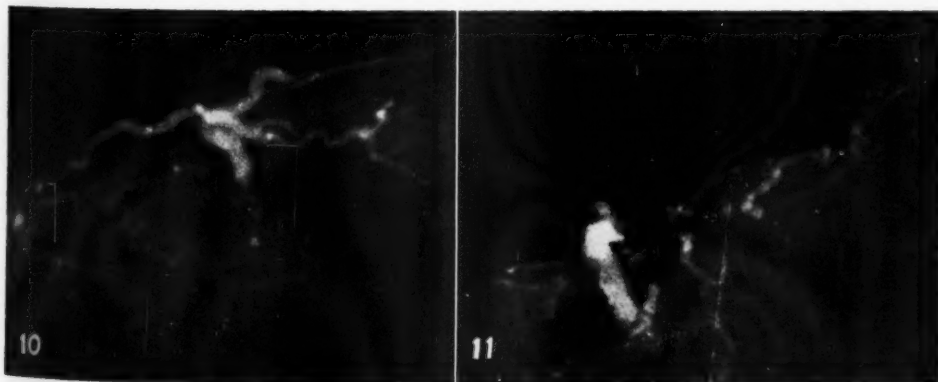


Fig. 10. Type I: Vasa vasorum running parallel to the surface of the aorta (man).  $\times 95$

Fig. 11. Type II: Vessels entering the wall of the aorta at right angles.  $\times 95$





Fig. 12. Type III: "Staircase" pattern.  $\times 110$

understood demonstration of fine vascular structures than routine serial sections.

**ACKNOWLEDGMENT:** We are grateful to Dr. L. S. Carstairs and Dr. J. A. Veiga Pires of the Royal Northern Hospital, London N. 7 (England) for their care in preparing the English text of this paper.

Rua Alexandre Herculano, 17  
Lisbon, Portugal

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#### SUMMARY IN INTERLINGUA

#### Studio Microangiographic del Vasa Vasorum del Aorta Thoracic

Usque recentemente le studio del vasa vasorum se faceva exclusivemente per medio del injection de colorantes, un methodo que permette le demonstration de

solmente le vasos superficial de plus grande calibres. Le autores es le primes qui ha usate le technica de microangiographia post plenation del vasos con substantia de

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contrasto. Illes describe lor technica e reporta studios in le aorta thoracic de canes e cadaveres. Illes opina que microangiographia es le methodo del methodos pro le demonstration del vasa vasorum.

Un frappante constation esseva le curso sinuose del majoritate del vasa vasorum, lo que es reguardate como un del medios que servi a attenuar le pression in le capillares del pariete arterial. Variationes regional esseva observate in iste configuration. Anastomoses esseva presente in le tunica adventitie inter le vasa vasorum que prende lor origine in adja-

cente branca collateral del aorta. Le vasos que forma le rete adventitie exhibiva varie arrangiamentos. Plures curreva parallel al superficie e emitteva branca que entrava in le profundor del tunica adventitie a angulos recte o oblique. Alteres descendeva in le tunica adventitie a angulos recte e emitteva branca parallel al superficie del pariete. Alteres ancora habeva le conformation de scalas con series de grados. Vasos que attinge le tunica medie es de multo micre calibre e se termina in le plus grande numero del casos in le tertio exterior de iste tunica.



## Photoconductance Crystals for Intracavitary Dosimetry<sup>1</sup>

EMANUEL G. TULSKY, M.D., JEN-TI CHEN, M.D., and ARTHUR FINKELSTEIN, M.D.

A SUPPLEMENTARY method for the detection and measurement of radiation is the use of photoconductance crystals such as cadmium sulfide and cadmium selenide, which are employed commercially in photoelectric operating assemblies, such as door openers, counters, burglar alarms, automobile headlight dimmers, etc.

These crystals are grouped with the semiconductors of electricity. Exposure to light or radiation reduces the inherent resistance of the crystal to the passage of current so that, by comparatively simple circuitry, the changes in resistance can be detected and recorded (Fig. 1). This resistance change is directly related to the quantity and quality of the stimulating agent—light or radiation. The small size of the crystals (in millimeters), their photoelectric properties, and high sensitivity make their application to clinical use intriguing.

While there are a number of reports (9, 10, 13) in the literature of experimental data concerning the use of the crystals as detectors of ionizing radiation, there are few studies in the medical field concerning practical clinical usage. In 1953, Mauldon and Martin (12) developed a cadmium sulfide crystal probe for measuring dose rates in the rectum following the insertion of radon for the treatment of carcinoma of the cervix. They have also reported (1955) on a needle probe using cadmium sulfide crystals for the interstitial measurement of the dose delivered to the axillary lymph nodes in patients with breast cancer. Stephens-Newsham and LaPalme (17) have used photoconductance crystals as a centering device in cobalt-beam therapy of the esophagus.

The purpose of the present study is the

correlation of the calculated dose delivered to a volume of tissue with the actual dose as determined by intracavitary detectors in the form of photoconductance crystals.

Commercially available intracavitary ionization chambers are usually employed for the direct measurement of the depth dose. Cadmium sulfide crystals, however, present several advantages which are of value clinically. Due to the relatively low impedance of the crystal, no difficulties are encountered in respect to leakage of charge, humidity, or length of cable, such as are found with small intracavitary thimble chambers. The photoconductance probes are relatively inexpensive—the probes, cable, and ratemeter having been assembled for less than \$100.

Our studies were based on commercially available cadmium sulfide crystals, obtained as a Clairex Corp. Cl-2 photocell, having overall dimensions of 14 mm. length and 5 mm. diameter. In use clinically in a light-proofed plastic shield, the probe measured 18 mm. in length and 7 mm. in diameter. The flexible coaxial type cable, to which the cell was attached, measured 4 mm. in diameter (Fig. 2). The unit is thus of such size that it can be readily passed into body cavities such as the nasopharynx, esophagus, uterine cervix, etc. Since any length of cable can be used, the recording apparatus can be located conveniently outside the treatment room while the photoconductance crystal is within the patient during therapy.

The initial difficulty encountered was the variation of axial response. For a given geometry, the change of photoconductance varied depending upon which aspect the crystal was presenting to the source of radiation. This was attributable to the irregular shape of the crystal as well

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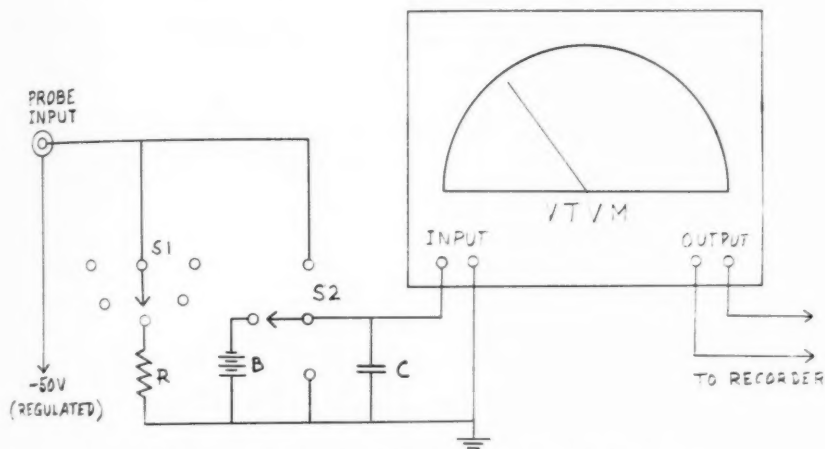


Fig. 1. Simplified diagram of the electronic circuit employed in the rate meter.

S<sub>1</sub>. Range selector switch (appropriate resistor R is selected for the input circuit to obtain the desired sensitivity. Typical values are 250,000 to 20 million ohms in steps of 1X, 2X, 5X, 10X, etc.).

S<sub>2</sub>. Function selector switch to facilitate zero adjustment, full-scale calibration, and measuring positions.

B. Four-volt mercury battery used as standard for full-scale calibration of the meter and recorder.

C. Damping capacitor to reduce AC hum pick-up and random resistance fluctuation of the crystal probe (a typical value is 0.01 mfd).

VTVM. Vacuum tube voltmeter capable of driving the pen recorder with provisions for zero and full-scale adjustments. The plate and filament supply voltages are stabilized to minimize the effects of line voltage fluctuations.

as the variations in absorption due to the tinned copper leads with their soldered wire. Although of less significance for single-field radiation, such a defect is serious in rotation techniques. This situation was largely corrected by mounting the crystal in a plane parallel to the long axis of the cell and placing copper foil directly over the more sensitive portions of the crystal between the copper leads, thereby reducing sensitivity in these areas (Fig. 3). The axial variation was found to be greatest in the measurements in air rather than those within the phantom. Higher qualities of radiation (above a 1 mm. Cu h.v.l.) gave a more uniform level of conductance than those in the range of superficial therapy (1 to 3 mm. Al h.v.l.).

In the non-medical literature (4, 6, 7, 9, 10) several additional drawbacks to the use of photoconductance crystals have been suggested, particularly the slow response to radiation, the changes in response due to aging, and the effects of temperature. At the relatively high dose



Fig. 2. Intracavity probe. CdS crystal photocell within light-proofed plastic shield plus flexible cable, which may be chemically sterilized.

rate employed in therapy the former is not significant, but it might limit the usefulness of the crystals for the measurement of short diagnostic exposures. The response time can be further minimized by the method of radiation biasing suggested by Hollander (7), who found that the response time is shortened by pre-

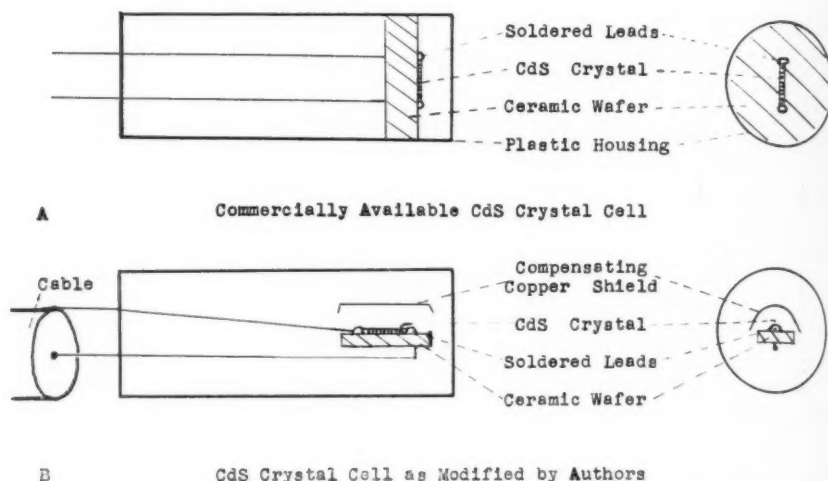


Fig. 3. Cadmium sulfide crystal cell, as commercially available and as modified by the authors.

exposing the crystal to radiation. We have carried out biasing by exposing the crystal to approximately 1,000 r immediately before use. This can be done readily and rapidly with the superficial therapy unit at a short target-crystal distance.

Aside from an initial change in response during the first month, we have found no significant changes due to aging during the subsequent year of use of the crystals, and early experimental work has been reproduced months later. The temperature coefficient of cadmium sulfide is approximately 0.1 per cent per degree centigrade and therefore negligible in clinical studies.

By means of a unit consisting of a crystal probe, ratemeter, and recorder (Fig. 4), studies with a Presdwood phantom were correlated with simultaneous depth dose measurements by a Victoreen thimble chamber. The qualities of radiation used ranged from a h.v.l. of 2.5 mm. Al to 3.9 mm. Cu. Curves were derived for the field sizes most frequently used in clinical practice (Fig. 5).

Within tissue at the depth usually encountered clinically in rotation therapy, and for the quality of radiation usually employed, the curve is relatively flat (Fig. 6). Thus, although there is a definite

energy dependence of the crystal, the clinical usefulness of the probe is not impaired. The plot of the crystal response (on an arbitrary scale using the deflection of the needle measured by the recorder divisions) as related to the depth dose readings showed that there was no strictly linear response to radiation in the qualities selected for study. We cannot, therefore, say that a recorder division is equal to a specific roentgens-per-minute calibration. The dose rate must be obtained from a complete curve calibrated against the depth of the probe in the phantom.

Johns' (11) tables of tumor-air ratios for rotation therapy dosimetry, as determined by ionization chambers, were found to be in essential agreement with our experimentally derived values of depth dose and can be plotted with the values obtained by the crystal studies (Fig. 7). This permits use of readings obtained by the photoconducance crystal without requiring actual calibration of the crystal against an ionization chamber.

One of the greatest sources of error in currently used radiation dosimetry is the employment of depth-dose data based on phantoms constructed of unit density material when the therapy is actually being directed at non-water-equivalent human tissues, the density of which varies from



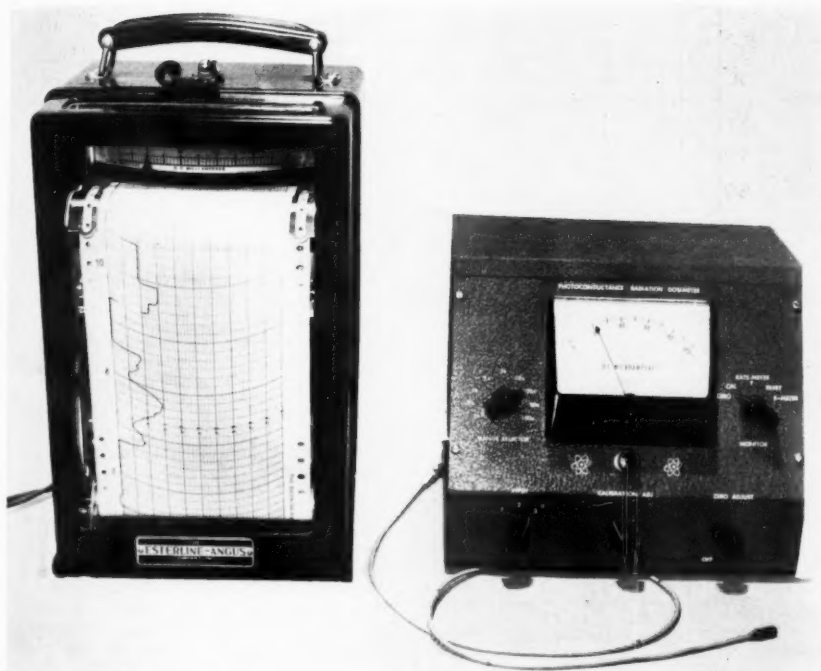


Fig. 4. Clinical unit. Crystal probe at end of flexible cable in foreground, attached to rate-meter. Pen recorder on left.

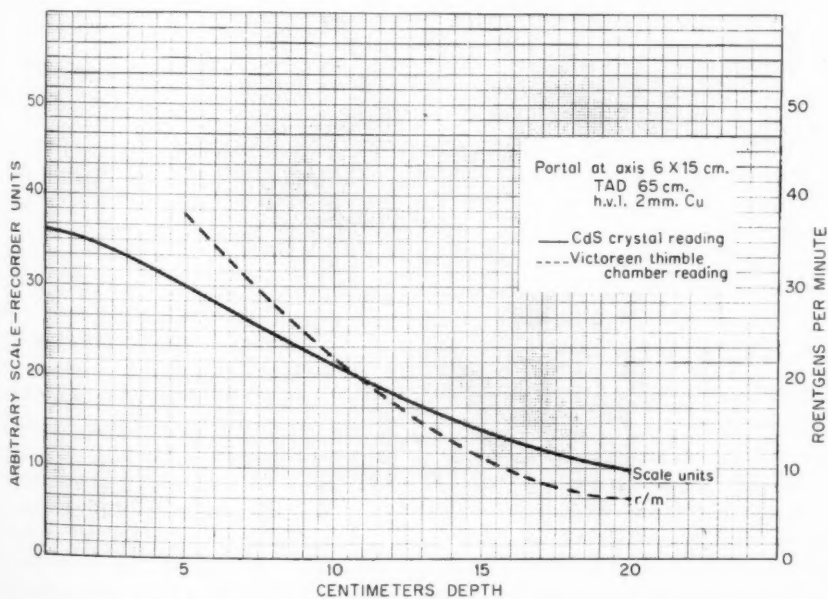


Fig. 5. Calibration curve. Dose rate at varying depths in phantom as determined by the Victoreen thimble chamber (dashed line) compared with arbitrary recorder units obtained with the photoconductance crystal probe (solid line).

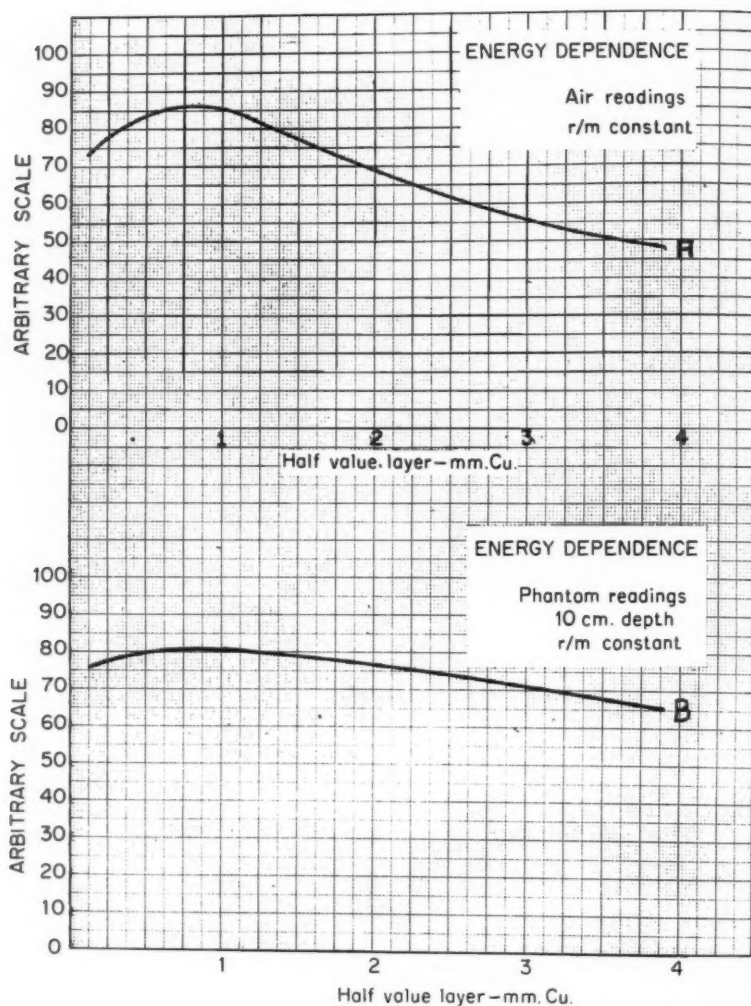


Fig. 6. Curve A shows variation in response of crystal in air with changes in quality of radiation, while  $r$  per minute remain constant. Curve B shows flattening of the curve when crystal is at 10 cm. depth in phantom; other factors as above.

approximately 0.25 (lung) to 1.85 (average bone), and the effective atomic number from approximately 6 (fat) to 14 (bone) (1, 3, 16).

Pfalzner (14) has attempted to correct these variations somewhat by reducing the patient's thickness to an estimated effective water thickness. His transit-rate measurements produced a contour of water which is roughly equivalent to the density of the patient. These transit-dose studies, however, were applied only to rotation therapy.

The intracavitary application of the cadmium sulfide probe enables us to determine dose rate actually being delivered to the site of interest. When the photoconductance crystal is exposed to radiation in a Presdwood phantom, the degree of deflection of the needle of the recorder varies with the thickness of material interposed between the x-ray source and the probe. By placing the crystal in a phantom or in a patient at an unknown depth and correlating the deflec-

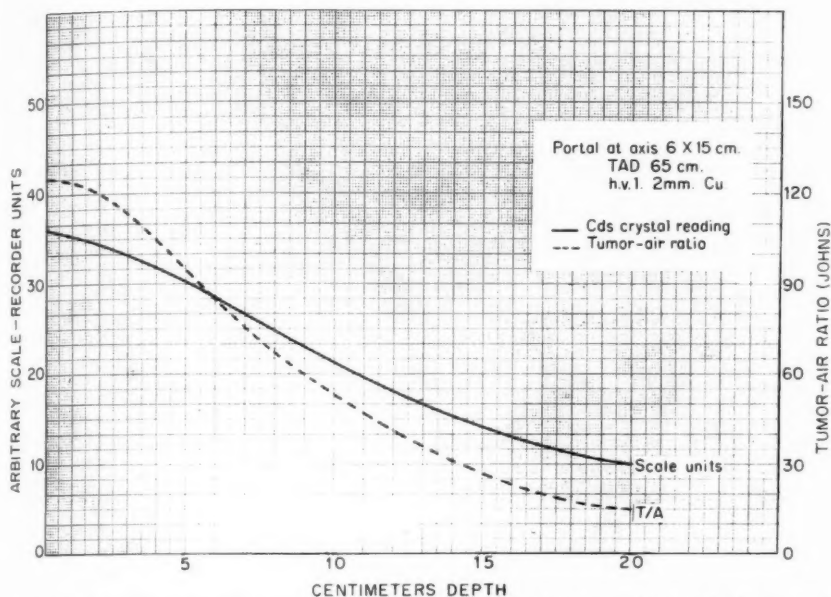


Fig. 7. Calibration curve. Tumor-air ratios (Johns) for varying depths (dashed line) compared with arbitrary recorder units obtained with the photoconductance crystal probe (solid line). This graph demonstrates the use of tumor-air ratio data obtained from Johns' charts as applied to curves obtained from the intracavitary crystal in the calculation of dose rates.

tion of the recorder needle with the calibration curves, the distance from the surface (or the skin) to the probe can be expressed as equivalent to a specific thickness of Presdwood.

In rotation therapy a continuous recording of dose rate can be obtained during the entire 360° of treatment (Fig. 8). The equivalent thickness in terms of centimeters of Presdwood can be determined at any point in a circle of rotation by measuring the degree of deflection and converting this figure to centimeters of Presdwood from the appropriate calibration curve (Figs. 5 and 7). By selecting multiple points at varying positions during rotation (usually 12 points, *i.e.*, at every 30° of rotation) and using the resulting thicknesses as radii extending from a point (corresponding to the location of the crystal in the patient), one can construct an equivalent contour in which lung, bone, and soft tissues are converted to a single density—that of Presdwood (Fig. 9). This contour may be compared with that representing the physical outline of the patient.

In thoracic irradiation, for example, the phantom contour will be reduced in size, with the greatest shrinkage occurring, as is to be expected, along those directions in which considerable lung tissue is traversed (Fig. 10).

The construction of the equivalent contour is a convenience but is not essential for the estimation of the dose delivered to the site of the crystal. From the graphs a direct roentgens-per-minute reading (Fig. 5) of the tumor-air ratio (Fig. 7) for each sector can be determined. The actual dose rate at the axis of rotation is found from the average of these sector values.

We have compared the dose rate as measured by the various technics in thoracic and pelvic rotational therapy. In a patient with carcinoma of the mid-esophagus, the lesion is located at the axis of rotation, where the dose rate as determined by conventional methods (tumor-air ratios applied to the patient's contour) is 15.7 r per minute. If one applies Johns' technic to the equivalent contour, the dose rate is 19.5 r per minute

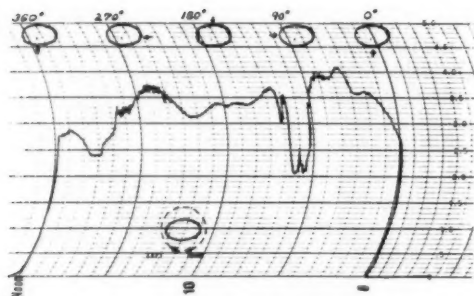


Fig. 8. Pen recording of photoconductive crystal response to 360° rotation of tube during rotational therapy of chest. Probe within the esophagus at axis of rotation. Field 6 × 15 cm. at axis, h.v.l. 2.0 mm. Cu, TAD 65 cm.

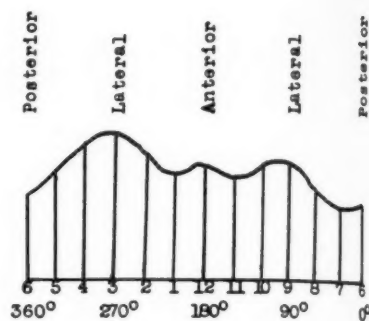
or 20 per cent greater than by conventional computation. Direct measurement using the crystal gives a dose rate of 19.2 r per minute. It is thus evident that applying the tumor-air ratio method to the equivalent contour is quite satisfactory, since it provides an estimated dose rate within 1.5 per cent of that measured by the crystal.

In a series of 11 patients with esophageal neoplasms there was a variation in the dose rate, as determined by the photoconductive crystal within the esophagus, from 10 to 32 per cent greater than the dose estimated by using the patient's body outline.

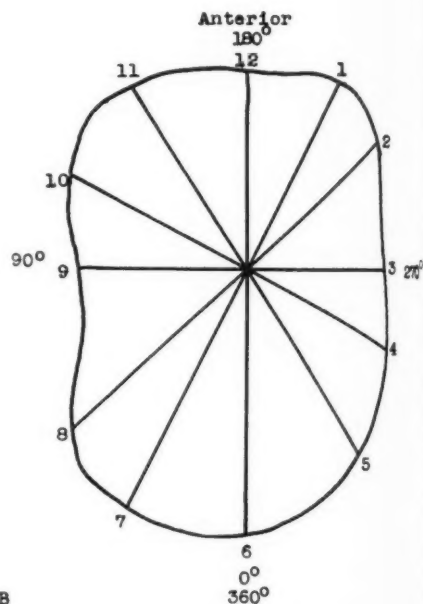
In a group of 14 patients undergoing pelvic irradiation (Fig. 11), the conventionally calculated dose ranged from 2 to 16 per cent greater than the actual dose delivered to the axis of rotation as determined by the photoconductive crystal or the equivalent contour.

Other workers (14, 15), using transit-dose methods, have found that the calculated dose in radiation to the head ranged from 3 to 6 per cent greater than the dose actually delivered. Using the crystal for direct measurements plus the equivalent contour concept, we have found a similar variation in two patients with nasopharyngeal lesions.

Although intensive studies have not been made, preliminary investigation confirms the work of others that photoconductive crystals are of value in intracavitary



A



B

#### EQUIVALENT CONTOUR

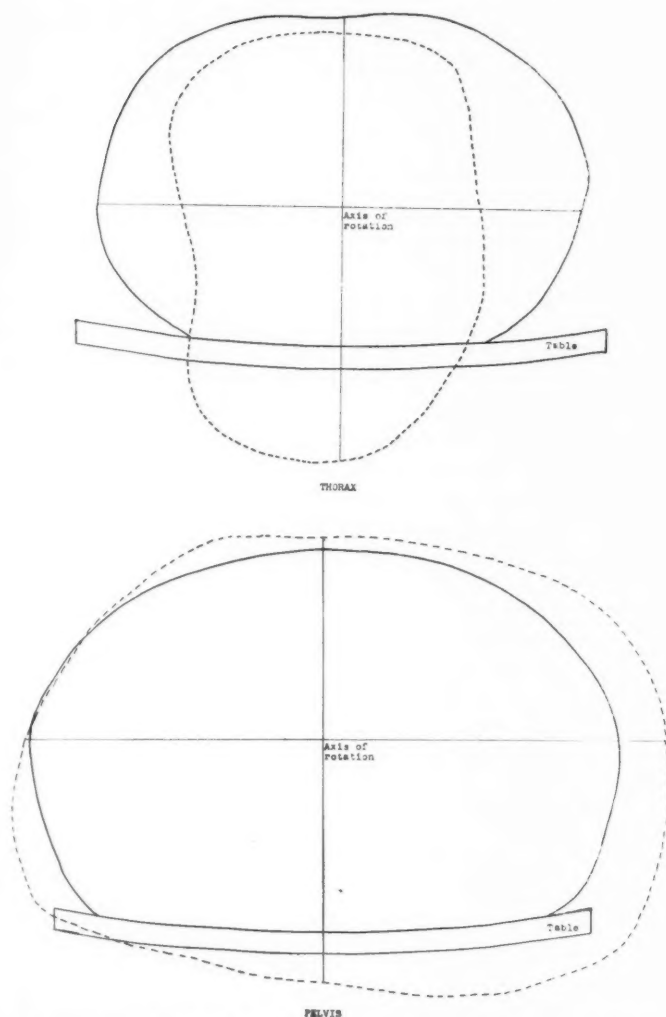
Fig. 9. A. Simplified pen recording of readings of depth dose rate obtained by CdS crystal at 30° intervals during 360° rotational therapy.

B. The equivalent contour obtained by converting the above readings (vertical lines) into centimeters of Presdwood, using calibration curves shown in Figures 5 or 7. The radii representing depth of probe vary inversely with the readings of depth-dose rate.

radium dosimetry. In gynecologic tumor patients the dose delivered to the bladder and rectum by intrauterine radium can be determined by the introduction of the crystal into the organ in question.

An attempt to apply this technic to diagnostic procedures is under way. For example, a solid conductance detector in

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Figs. 10 and 11. Comparison of the contour representing the physical outline of the patient (solid line) with the Presdwood equivalent contour (dashed line) as obtained through the use of the CdS crystal probe.

Fig. 10 (above). In thoracic radiation. The probe is in the esophagus at the axis of rotation.

Fig. 11 (below). In pelvic radiation. The probe is in the posterior fornix at the axis of rotation.

the uterus during the course of fluoroscopy and film study of the stomach and duodenum should indicate rather accurately the quantity of gonadal radiation received. Increased technical problems are apparent because of the energy dependence of the crystal as well as the relatively short exposure time of the diagnostic procedures. However, with modifications suggested by

Hollander (8) and the development of new crystals such as those of Czyzak *et al.* (4), the problems are not insurmountable.

#### SUMMARY

The principle of photoconductance has led to an inexpensive supplementary technique for the direct measurement of ionizing radiation. The small size of the detector



crystal lends itself to intracavitary dosimetry, particularly for problems in rotation therapy. In various locations, particularly lesions of the esophagus, the dose rate can be determined at the edges of the field along the axis of rotation, as well as at the intersection of the central ray with the axis of rotation, as calculated by conventional methods. By the use of this method, the actual dose delivered to the patient during radiation can be measured directly in any patient in whom there is external access *via* artificial passages (-ostomies, drainage tubes, etc.) as well as natural orifices.

An alternate method in the calculation of dosage in rotation therapy is the application of tumor-air ratios to the equivalent contour in which the patient is "converted" to a single density—that of Presdwood. Thus correction is automatically made for differences in transmission through lung, bone, and soft tissue.

Graduate Hospital  
19th and Lombard Sts.  
Philadelphia 46, Penna.

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## SUMMARIO IN INTERLINGUA

## Crystallos Photoconductive in Dosimetria Intracavitari

Es describe un methodo supplementari pro le detection e mesuration de radiation per le uso de crystallos photoconductive, como sulfato o selenuro de cadmium.

Le micre dimensiones del crystallo detectori facilita su uso in le dosimetria intracavitari, specialmente pro problemas de therapia rotational. In varie locationes, specialmente in lesiones del esophago, le dosage pote esser determinate al margines del campo al longo del axe de rotation e etiam al intersection del radio central con le axe de rotation (como illo

es calculate per methodos conventional). Per le uso del presente methodo, le dose que es de facto delivrate al patiente durante le radiation pote esser mesurate directamente in omne caso in que il existe un via de accesso per passages artificial (-ostomias, tubos de drainage, etc.) e etiam per orificios natural.

Un altere methodo in le calculation del dosage in therapia de rotation es le application del proportion tumor/aere a un "contorno equivalente" in que omne le tissus del patiente es reducite a un sol densitate, i.e. le densitate de Presdwood.

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# Exfoliative Cytology in Radiotherapy of Oral Cancer

## Its Use in the Diagnosis of Residual Carcinoma<sup>1</sup>

W. UMIKER, M.D., R. RAPP, M.D., I. LAMPE, M.D., and H. B. LATOURETTE, M.D.<sup>2</sup>

THE EXACT biological status of an oral carcinoma is often difficult to assess on the completion of irradiation. Residual neoplasm may be suspected because of persistent induration, excrescence, or ulceration. The radiation reaction, usually intense at this time, makes interpretation of these findings uncertain. Immediate biopsy is not advisable and determination of cancer cell viability by histologic examination may be difficult. This paper reports a study undertaken to ascertain the value of oral smears in the diagnosis of residual neoplasm following irradiation for oral cancer.

### MATERIAL AND METHOD

Direct smears were taken from the sites of 25 irradiated oral carcinomas of the floor of the mouth, palate, gingiva, tongue, tonsil, and glossopalatine fold. The smears were obtained during and at the completion of treatment, which was usually administered over periods of five to seven weeks. In 14 of the cases smears were also taken during the post-irradiation months.

The smears were fixed in ether-alcohol, stained according to the Papanicolaou technic, and examined for the presence of malignant cells, with no attempt at differentiation of viable from nonviable cells.

### RESULTS

The cytologic findings during irradiation have been published elsewhere (1-4).

In 16 of the 25 patients malignant cells were still present in the smears at the completion of treatment; the smears from 5 others were equivocal, and in the remaining 4 the smears were negative (Table I). As shown in Table I, the presence or absence of residual neoplasm, clinically, had no

TABLE I: ORAL SMEARS AT COMPLETION OF TREATMENT

Cytology	Clinical Evaluation		Total
	Residual Neoplasm	No Residual Neoplasm	
Positive	8	8	16
Suspicious	2	3	5
Negative	2*	2	4
TOTAL	12	13	25

\* Subsequent smears were positive within a few weeks following treatment.

effect on the cytologic findings in smears taken immediately following treatment. Negative and positive results occurred with equal frequency in each group.

Cytologic examination two to ten weeks later showed no correlation with observations on completion of treatment, and more accurately reflected the clinical status (Table II). The 2 patients whose smears

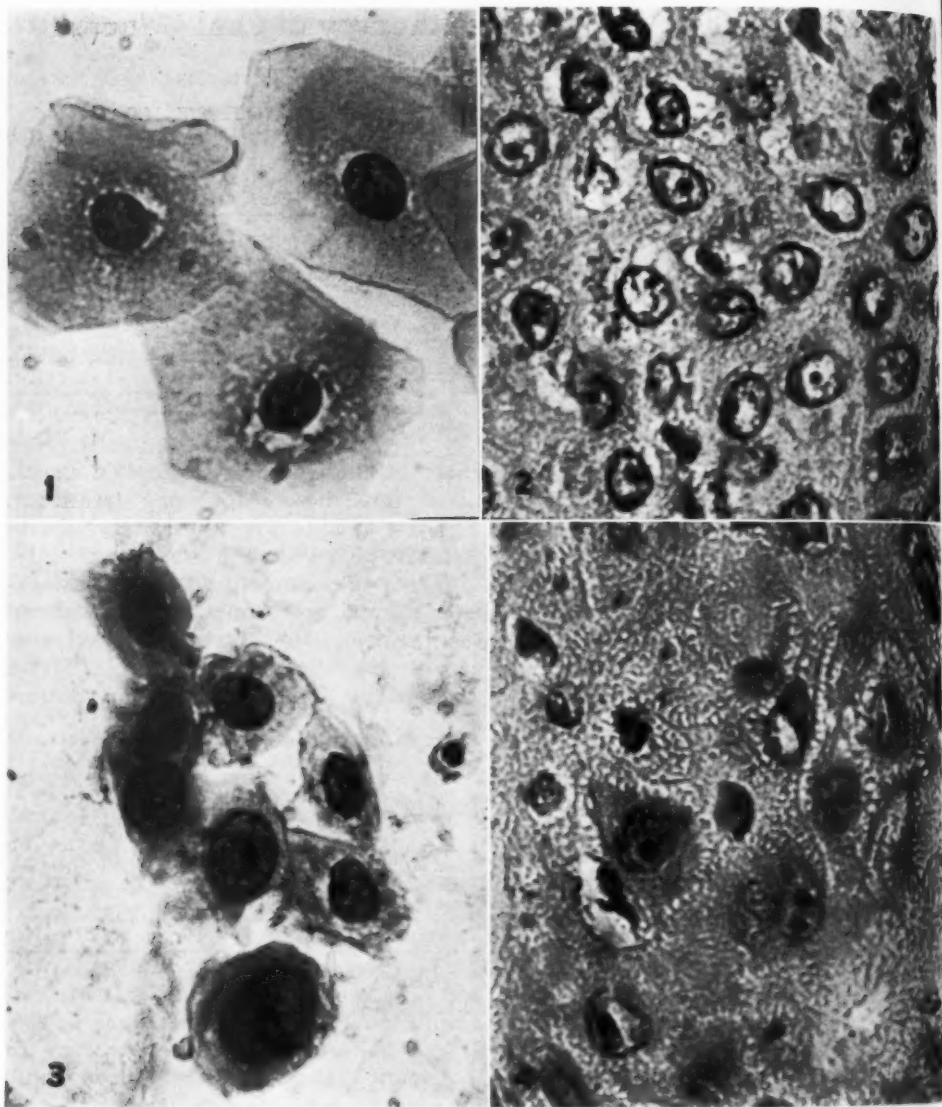
TABLE II: ORAL SMEARS TAKEN SEVERAL WEEKS AFTER TREATMENT

Cytology	Clinical Evaluation		Total
	Residual Neoplasm	No Residual Neoplasm	
Positive	7	0	7
Suspicious	1	1	2
Negative	0	5	5
TOTAL	8	6	14

had been negative at the end of treatment, despite obvious residual neoplasm (Table I), now had smears which were positive for malignant cells. On the other hand, malignant cells disappeared from the smears of 5 of the 13 patients with no clinical evidence of residual neoplasm. Smears from 1 other patient were suspicious for malignant cells, and the remaining 7 patients either did not have the benefit of follow-up smears or were not evaluated cytologically until many months later.

<sup>1</sup> From the Departments of Pathology and Radiology, Veterans Administration Hospital and The University of Michigan Medical School; and the Alice Lloyd Crocker Radiation Therapy Center, Ann Arbor, Mich. Accepted for publication in October 1959.

<sup>2</sup> At present in the Department of Radiotherapy, Iowa State University, Iowa City, Iowa.



Figs. 1-4. Case III.

- Fig. 1. Benign irradiated squamous cells in oral smear.  $\times 780$   
 Fig. 2. Histologic section from irradiated mucosa adjacent to neoplasm.  $\times 780$   
 Fig. 3. Oral smear showing malignant squamous cells. Note variation in size of nuclei and prominence of nucleoli.  $\times 780$   
 Fig. 4. Histologic section showing residual well differentiated squamous-cell carcinoma.  $\times 780$

The following cases illustrate the type of information obtained by this form of cytologic study.

**CASE I:** An infiltrating, well differentiated squamous-cell carcinoma in the right lower gingivobuccal sulcus was given external and peroral x-

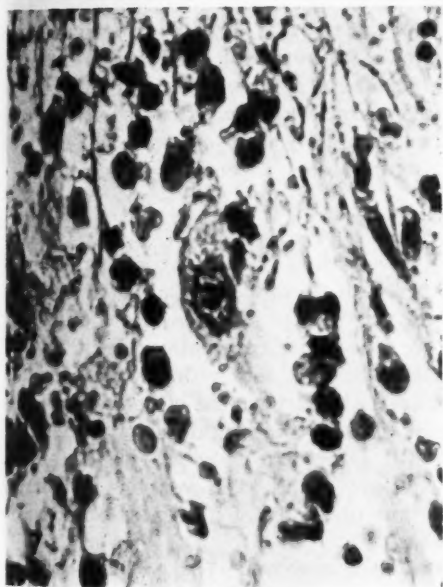
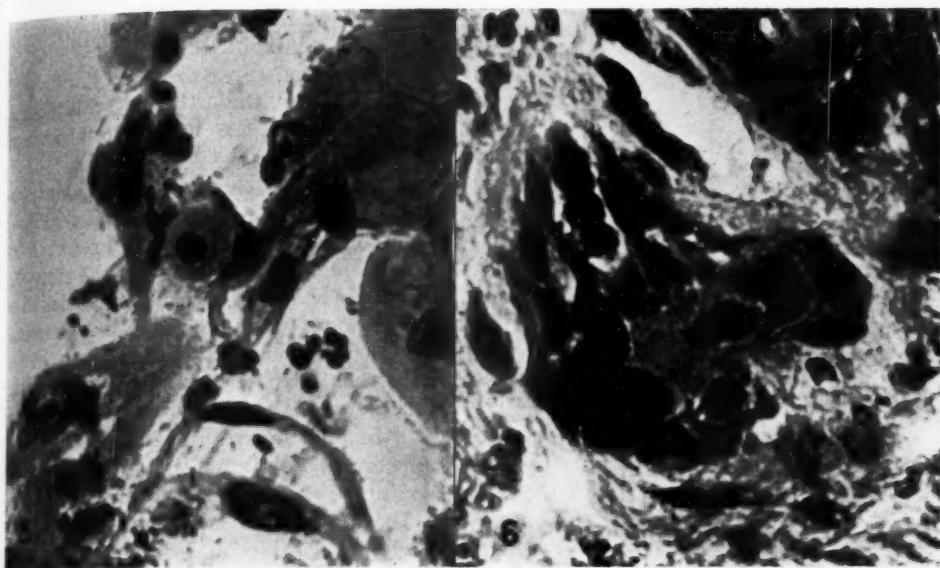
irradiation. At the completion of treatment there remained only a small, granular irregularity, which was thought to represent granulation tissue. Smears taken at the completion of treatment and at monthly intervals thereafter, however, all contained malignant cells. A biopsy nine months after treatment disclosed unequivocal carcinoma.

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Figs. 5-7. Case III.

Fig. 5. Poorly differentiated malignant squamous cells in oral smear.  $\times 780$

Fig. 6. Histologic section showing residual anaplastic squamous-cell carcinoma.  $\times 780$

Fig. 7. Degenerating malignant squamous cell in exudate covering ulcerated neoplasm.  $\times 780$

*Comment:* This case illustrates the occasional difficulty in the clinical recognition of residual neoplasm. Clinically

the appearance was not that of persistent neoplasm, but cytologically residual carcinoma was present.

**CASE II:** A superficial squamous-cell carcinoma in the left glossopalatine fold received external x-irradiation. At the completion of treatment there was persistent granularity at the inferior pole of the anterior tonsillar pillar. An oral smear at that time was positive, but subsequent smears were persistently negative. One year later there was no residual neoplasm and the granular area had decreased in size.

*Comment:* Clinically the post-treatment appearance resembled that in the first case, but the cytological examinations indicated that the process was not neoplastic.

**CASE III:** A well differentiated squamous-cell carcinoma in the right glossopalatine fold received external and peroral x-irradiation. A small ulcerated area remained which, clinically, was thought to represent an area of radionecrosis. Follow-up smears, however, were positive (Figs. 1-7), and a biopsy during the eighth month after irradiation confirmed the presence of carcinoma.

**CASE IV:** An undifferentiated-cell carcinoma in the left tonsil was treated by external irradiation, with complete disappearance of the mass. Smears were positive for malignant cells at the completion of treatment but subsequently became negative and remained so at twelve and nineteen months. Cervical metastases appeared at twenty months, at which time the primary site contained no visible



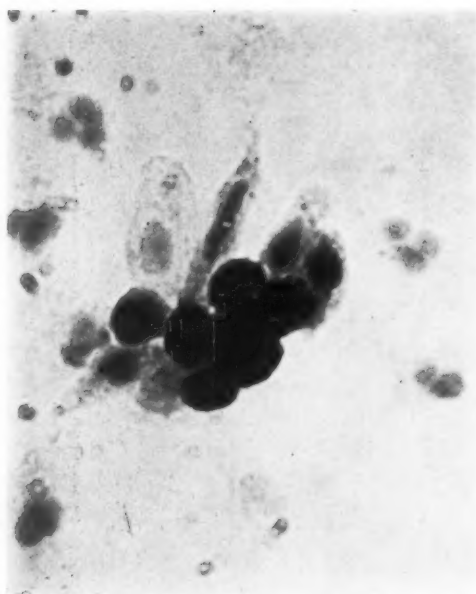


Fig. 8. Case IV. Oral smear showing cluster of undifferentiated malignant cells from recurrent carcinoma of tonsil.  $\times 780$

neoplasm, but no smears were taken. At thirty-two months a small nodule appeared at the junction of the tonsil and the base of the tongue. Despite the submucosal appearance of this lesion, abundant undifferentiated malignant cells were found in direct smears (Fig. 8). Biopsy disclosed carcinoma similar to that previously seen.

*Comment:* A recurrence two and one-half years after treatment illustrates the possible value of oral smears in the detection of recurrent carcinoma.

#### DISCUSSION

The results of this preliminary study suggest that oral smears are of little or no prognostic value when taken immediately after completion of irradiation of oral cancer. The presence of malignant cells in these smears does not mean irradiation failure, and their absence during this phase does not exclude the presence of residual neoplasm. Similar observations have been reported by the Grahams (5), who noted that women with irradiated cervical cancers might have malignant cells in the vaginal smears for several weeks following treatment and yet be cured.

There was no correlation between the cytologic findings at the completion of treatment and those observed during subsequent weeks, when the oral smears accurately indicated the presence or absence of residual neoplasm.

Since most of the patients without residual disease have not been followed long enough for the development of recurrences, the value of oral cytology in the early detection of recurrent carcinoma remains to be ascertained. The success of such examinations will depend largely upon whether or not the recurrent tumor involves the mucosa. It should be noted that, in Case IV, the mucosa over a recurrent carcinoma appeared to be intact, yet the oral smears contained abundant malignant cells.

In the early phases of this study there was considerable difficulty in interpreting some of the atypical cells in the smears. The use of rigid cytologic criteria usually permitted a definite diagnosis, although considerable experience is necessary for proper interpretation of some smears, and the adoption of a "suspicious" category was necessary in certain instances.

#### CONCLUSIONS

1. Smears taken at the completion of radiation therapy for oral carcinoma were of little or no practical value in determining the presence of residual neoplasm.
2. Smears taken during the first few weeks after treatment correlated well with the clinical course and biopsy findings.
3. Oral cytology provides a simple, painless, rapid, and reliable tool in the follow-up study of irradiated oral carcinomas.

**ACKNOWLEDGMENT:** The photomicrographs reproduced in this article were taken by Mr. Robert Logan.

Veterans Administration Hospital  
2215 Fuller Road  
Ann Arbor, Mich.

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## SUMMARIO IN INTERLINGUA

## Cytologia Exfoliative in le Radiotherapia de Cancere Oral

*Su Uso in le Diagnose de Carcinoma Residue*

Pro verificar le valor de frottis oral in le diagnose de neoplasma residue post irradiation pro cancro oral, frottis directe esseva prendite ab le sitios de 25 irradiate carcinomas oral al fundo del bucca o al palato, gingiva, lingua, tonsilla, o plica glossopalatin, durante le curso del tractamento e al momento de su completion. In 14 casos, frottis esseva etiam prendite durante plure menses post le irradiation. Le frottis esseva fixate in ethere e alcohol, tincturate secundo le technica de Papanicolaou, e scrutinate pro le presentia de cellulas maligne.

Esseva trovate que le frottis prendite al tempore del completion del radiotherapia pro carcinoma oral esseva de pauc o nulle valor practic in determinar le presentia de neoplasma residue, durante que le frottis prendite durante le prime septimanas post le tractamento esseva ben correlationate con le curso clinic e le constataciones biptic.

Es concludite que cytologia oral provide un simple, indolor, rapide, e fidel medio de controlo ulterior in le studio de irradiate carcinomas oral.

Quatro casos es reportate.



# Calorimetric Measurements of Bone/Tissue Absorption Ratios

PAUL N. GOODWIN, Ph.D.<sup>2</sup>

THIS PAPER will describe some calorimetric measurements of the energy absorbed in several tissue-equivalent materials exposed to x-radiation of 200 and 230 kv. These measurements are of interest for a number of reasons, since, despite the increasing use of supervoltage equipment, the majority of treatments are still given in the so-called high-voltage region of 200 to 250 kv; and for x-rays of this energy

side. The thermistor was connected as one arm of a Wheatstone bridge, and the bridge unbalance was detected by a galvanometer and twin-tube photocell amplifier.

A description of the calorimeter and of the method of making measurements has previously been published (2).

The x-ray unit used for these studies was a Westinghouse 250-kv constant-potential generator. Measurements were

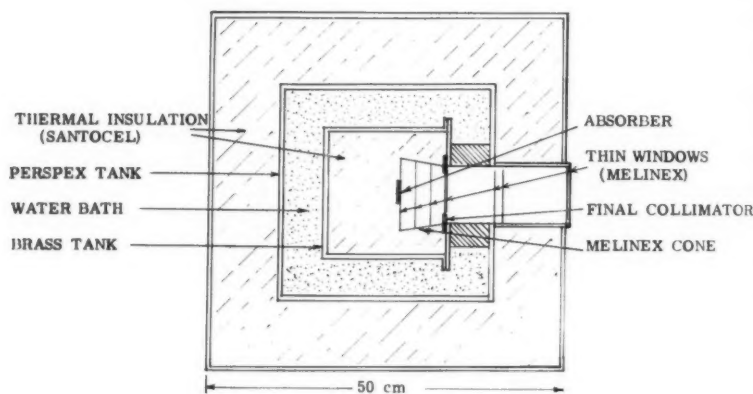


Fig. 1. Horizontal cross section of the calorimeter.

or lower there is a very considerable difference in the energy absorption in substances of different atomic composition, such as soft tissue and bone.

The calorimeter used for these measurements was originally designed to measure the total energy in beams of x and  $\gamma$ -rays. Its general layout is shown in Figure 1. A series of thin windows, totaling about 10 mg./sq. cm., allowed the x-ray beam to reach the absorbers with negligible attenuation. The absorbers were thin disks, 1 to 4 mm. thick and 5 to 8 cm. in diameter; they were suspended on a Melinex film, as shown. The temperature rise in an absorber was detected by means of a thermistor embedded in it or attached to the out-

made with four different qualities of x-rays, covering the range of half-value layers normally used in high-voltage therapy. Table I gives the factors used and the measured half-value layers.

TABLE I: FACTORS FOR THE FOUR X-RAY BEAMS USED FOR THESE MEASUREMENTS

Kv	Filter (mm.)	h.v.l. (mm. Cu)	r/Min. (50 cm.)
200	0.5 Cu + 1 Al	1.1	62
230	1 Cu + 1 Al	1.9	62.5
230	2 Cu + 1 Al	2.5	41
230	1 Sn + 0.5 Cu + 1 Al	3.2	27.3

Two absorbers roughly equivalent to soft tissue were made, one from Perspex and the other from polystyrene. The

<sup>1</sup> From the Physics Department, Institute of Cancer Research, Royal Cancer Hospital, London, England. Accepted for publication in October 1959.

<sup>2</sup> Present address: Department of Radiology, Johns Hopkins Hospital, Baltimore, Md.

effective atomic number of Perspex lies between that of muscle and that of subcutaneous fat, while that of polystyrene is about the same as of muscle. The atomic number and the electrons per gram of aluminum are close to those given for bone by Spiers (4); thus aluminum absorbers were used to simulate bone.

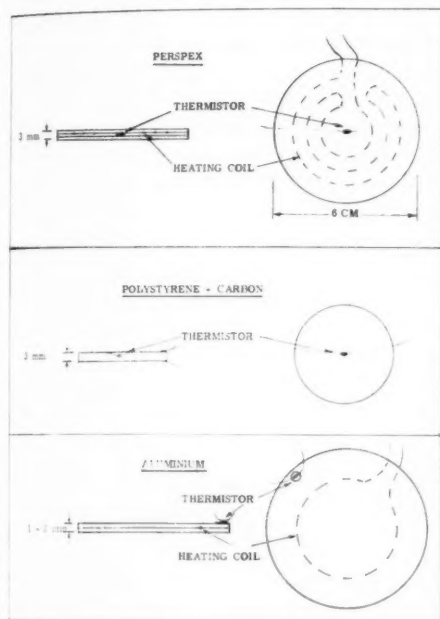


Fig. 2. Construction of the absorbers used to simulate soft tissue and bone.

The Perspex absorber was made from three 1-mm. pieces of Perspex cemented together. Embedded in the central piece was a Stantel type M thermistor, removed from its copper disk. A heating coil of a few loops of No. 45 copper wire was placed between the first and second pieces. This coil did not warm the Perspex uniformly and it was not used for calibration purposes, but merely to give an indication of the consistency of the readings, as it had previously been found that the apparent calorimeter sensitivity could change under different conditions of internal temperatures.

The second type of absorber was a disk of an electrically conducting plastic, made

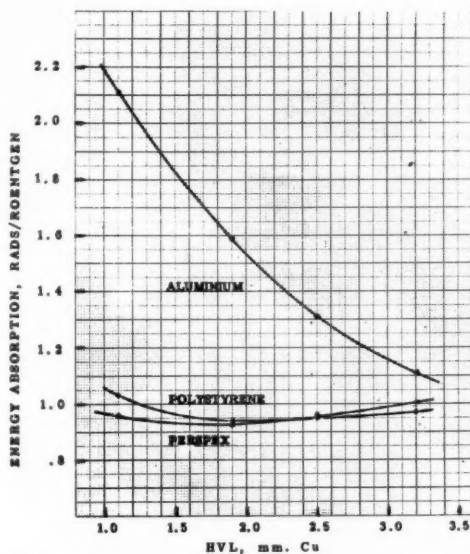


Fig. 3. Measured energy absorption in the three types of absorbers.

by mixing two parts of polystyrene moulding powder and one part of powdered graphite and shaping under heat and pressure. Several disks were made, each about 3 mm. thick and 5 cm. in diameter, the faces being coated with colloidal graphite to make them conducting. The disks then had a resistance of several hundred ohms between faces; a current of the order of one milliamperere warmed the disk about the same amount as did an x-ray beam.

The construction of these absorbers and also of the aluminum absorbers is shown in Figure 2.

Four aluminum absorbers were constructed, each about 9 cm. in diameter, with total thicknesses of about 1, 1.5, 2, and 3 mm. In each case two pieces of aluminum were fastened together with a heating coil between them, and a type M thermistor was attached to the outside near the edge of the disk, so as to be outside the area being irradiated. Four thicknesses were used in an attempt to determine any effects due to attenuation or back-scatter, but the different thicknesses gave identical values for absorption per gram.

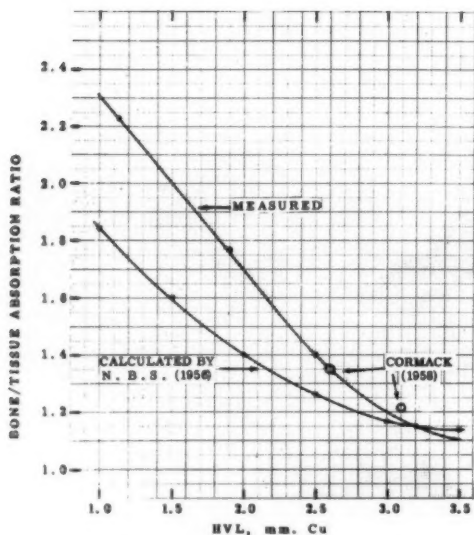


Fig. 4. Bone to soft-tissue absorption ratios. The upper curve was obtained from the measured values shown in Fig. 3; the lower curve from the data given in *Handbook 62* (3), Fig. 8. The circles are the corresponding ratios calculated from the spectral measurements of Cormack *et al.* (1).

Each of the three different types of absorber was irradiated with x-ray beams of four different qualities. The results are shown in Figure 3. Here the three curves show the energy absorption per gram per roentgen, where the roentgens represent the beam intensity as measured in air. Since for the Perspex absorber the absolute values could not be determined, the results were normalized to the calculated value for the 3.2-h.v.l. beam. For such a heavily filtered beam, the absorption in light elements is almost entirely Compton, and thus it depends only on the number of electrons per gram, which may be calculated quite accurately. The other points on the curve then represent the measured variation in absorption from beams of decreasing half-value layers. The slight increase between 2 and 3 mm. h.v.l. is to be expected if absorption were essentially all Compton, since the true part of the Compton absorption coefficient is rising slightly in this region.

The significance of these results is best shown by plotting the ratio of the absorption in bone to absorption in soft tissue

for each of the beams used. This ratio is shown as the top curve in Figure 4.

The variation in this ratio can also be calculated, using the data in the National Bureau of Standards *Handbook 62* (3). Here the calculated absorbed doses per roentgen in muscle and in bone are given for various primary x-ray spectra. The calculated ratios are shown as the lower curve in Figure 4.

The measured change in the absorption ratios is thus seen to be somewhat greater than that calculated. The chief cause of this discrepancy is probably the uncertainty in the x-ray spectra used to obtain the calculated ratios. Some of the data in *Handbook 62* are based on spectra measured by Cormack *et al.* in 1955 (3), but these authors have recently published a revision of their measurements (1). The ratios calculated from Cormack's revised spectra are shown as the two circles in Figure 4 and are seen to be in good agreement with our measured ratios. Spectra used for beams having half-value layers of less than 2 mm. copper were calculated by Kramers' method, and in this region photoelectric absorption becomes increasingly important, so that small errors in the spectrum could lead to large errors in the calculated absorption values. Thus it seems reasonable that measured ratios could differ appreciably from calculated ones.

It should be pointed out that these ratios, both measured and calculated, refer only to the primary x-rays. The ratios at a depth in tissue will generally be somewhat larger because of the presence of scattered radiation; how much larger will of course depend on the field size. We have made some attempts to measure these ratios 2 cm. deep in Mix D, a tissue-equivalent wax, but we were able to do this for only small fields, where we found the ratios no larger than the primary ones. But the spectra measured by Cormack at various depths in water show larger ratios for large fields.

These measurements of energy absorption provide the values for rads per roentgen in the 250-kv region, and they also

serve to emphasize the desirability of using heavily filtered beams at this energy, particularly if the treatment field includes any bone near the surface. For example, if an x-ray beam had a h.v.l. of 1.5 mm. Cu, then the dose to bone, that is, the energy absorption per gram, would be at least twice the dose to soft tissue, whereas if the same beam were used with enough filtration to give a h. v. l. of 3 mm. Cu, then the dose to bone would be only about 1.2 times that to soft tissue. Thus it is clear from these curves that more uniform dose distributions and much less danger of overdose to bone will result from using enough filtration to give half-value layers of about 3 mm. Cu, rather than only 1 or 2 mm.

ACKNOWLEDGMENTS: The author wishes to thank Professor W. V. Mayneord for suggestions concern-

ing this project. This paper is based on material included in a dissertation submitted to the University of London in partial fulfilment of the requirements for the Ph.D. degree. This work was performed while the author was a U. S. Public Health Service Research Fellow of the National Cancer Institute.

Department of Radiology  
Johns Hopkins Hospital  
Baltimore 5, Md.

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## SUMMARIO IN INTERLINGUA

## Mesurationes Calorimetric del Proportion de Absorption Inter Osso e Tissu

Esseva effectuate mesurationes calorimetric del energias absorbite in plure tissu-equivalente materiales exponite a un radiation X de 200 e 230 kv. Duo absorptores grossiermente equivalente a tissu molle esseva usate, le un de Perspex e le altere de polystyrena. Absorptores de aluminio esseva usate pro simular osso. Le absorptores de iste varie typos esseva irradiate con fascas de radios X de quatro differente qualitates.

Tal mesurationes del absorption de energia provide le valores del rads per

roentgen in le region de 250 kv. Illos etiam servi a sublinear le desirabilitate del uso de fortemente filtrate fascas a ille nivello de energia, particularmente si le campo de tractamento include osso proxime al superficie. Il es clar ab le resultatos que plus uniforme distributiones de dosage e un grandemente reduce riscos de excessos de dosage al osso resulta ab le uso de un filtration sufficiente a producer un spissitate de medie valor de circa 3 mm de cupro, plus tosto que solmente 1 o 2 mm.



## Episternal Bones

### A Case Report<sup>1</sup>

WEBSTER H. BROWN, M. D.

**E**PISTERNAL BONES, also known as suprasternal bones or ossa suprasternalia, are found on or just above the posterior margin of the manubrium. They are anomalous structures which may be single or paired, small or large, fused or free; they vary considerably in shape and may articulate with the manubrium or with one another. Caffey has included a case in his text on *Pediatric X-Ray Diagnosis*, with illustrations (1). The only other case which could be found in the English literature, with an illustrative roentgenogram, was that of Morris (4).

These ossicles are probably of little clinical significance unless involved by infection, trauma, or arthritic change, or unless a single and somewhat atypical episternal bone is mistaken for a possibly significant lesion.

In 1937, Cobb (2) reviewed comprehensively the anatomical literature on this subject and cited 91 references. The paper describes so well the various aspects of the anomalous ossicles that it is probably the authoritative source. The variation and incidence of suprasternal bones and the form of the superior manubrial border were investigated on 2,188 human and 107 anthropoid sterna in the Hamann Museum of Western Reserve University, a larger and better documented collection of material than had hitherto been available. The following notations are extracted from the summary of Cobb's paper.

"Roentgenograms of 1,010 of the human sterna taken before maceration and with the clavicular ligaments still attached made possible the detection of minute ossicles otherwise lost. Comparison of manubria with their roentgenograms demonstrated that the dry manubrium may show no evidence of a suprasternal bone which was present. The incidence of separate ossicles was relatively higher in our roentgenographed series than in that composed of dry bones alone. Estimates of incidence based



Fig. 1. Sternum and episternal bones; author's case.

on macerated material are, therefore, unreliable. "Suprasternal bones range in size between that of a small shot and an average female lumbar bone. An average is: length 10.4 mm., breadth 10.4 mm., height 7.3 mm.

"Variation: Suprasternal bones occur in pairs and singly. They may separate, forming a diarthrodial joint with the manubrium complete with articular cartilage and synovial membrane; they may be united to the manubrium by synchondrosis or as small nodules they may be ensconced within the suprasternal ligaments and have no contact with the manubrium. The ossicles exhibit various degrees of fusion with the manubrium and with each other, almost complete incorporation in the former being sometimes detectable. When fusion occurs can only be surmised but is probably early. Paired suprasternal bones may be of subequal size and symmetrical form and position on the manubrium or of unequal size and asymmetrical arrangement. One element may be separate and the other fused.

"Incidence: The roentgenograms showed separate or fused suprasternal bones in 6.8 per cent. of 544 adult whites and 2.2 per cent. of 466 adult Negroes. The incidence was highest in 79 white

<sup>1</sup> Accepted for publication in July 1959.

females, 7.6 per cent.; lowest in 132 Negro females, 0.0 per cent. (One case of ossicles in a female Negro was found in the second series.) For the males, the percentages were: 465 whites, 6.8; 344 Negroes, 3.0. Thus the ossicles appear three times more frequently in whites than in Negroes. They are more than twice as frequent in white males as in Negro males, and nearly eight times more frequent in white females than in Negro females.

**"Frequency of Types of Ossicles:** About two-thirds of the suprasternal ossicles which occur are separate and one-third fused. Paired ossicles are slightly more frequent than single in the separate group, but paired and single are of approximately equal frequency among fused ossicles. The separate ossicles occur about 30 per cent more often in whites than in Negroes.

**"Associated Anomaly:** The suprasternal elements in this series revealed no particular association with any anomaly or defect in the sternum, and were in no case associated with a cervical rib."

Figure 1 illustrates a case seen by the author in which such ossicles presented in unusually striking fashion. The episternal bones are best seen in the oblique projection, which portrays them with a minimum of overlying and obscuring densities. Several foreign authors (3-6) have devised specialized technics for optimum visualization. The advent of the laminagraph renders such methods unnecessary.

# SUMMARY

1. A brief discussion of episternal bones is presented.

2. A roentgenogram is reproduced from a case with moderately large, well ossified bilateral symmetrical episternal bones, with no related symptoms.

11 East Biddle St.  
Baltimore 2, Md.

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# SUMMARIO IN INTERLINGUA

## Ossos Episternal: Reporto de Un Caso

Ossos episternal, etiam cognoscite como ossos suprasternal, es structuras anormal trovate sur o justo supra le margine posterior del manubrio. Illos occurre sol o in pares, micre o grande, fusionate o libere. Illos varia in conformation e pote esser in articulation con le manubrio o le unes con

le alteres. Il es probabile que illos es de pauc signification clinic.

Es illustrate un caso vidite per le autor in que le ossiculos se presentava de maniera inusualmente frappante. Iste ossos anormal es le melio demonstrate in expositiones oblique.

## Pulmonary "Coin" Lesion of Unusual Pathology<sup>1</sup>

R. PAUL, M.D., F.R.F.P.S.

THE DIAGNOSTIC problem of single discrete lesions of the lung is well recognized (1, 3, 5, 7). The subject has recently been comprehensively dealt with in *Bronchopulmonary Diseases* edited by Naclerio (8). There is general agreement as to the difficulty of determining the pathology of these lesions when revealed by x-ray. Their management, too, presents a prob-

amed clinically and radiologically each year. Discrete single lesions of the lung are periodically observed. Hitherto all have fallen into one or other of the categories usually encountered. The case described below, however, is unique. The single "coin" lesion in this instance was due to a pulmonary infarct caused by an intra-arterial schistosome. Although in-

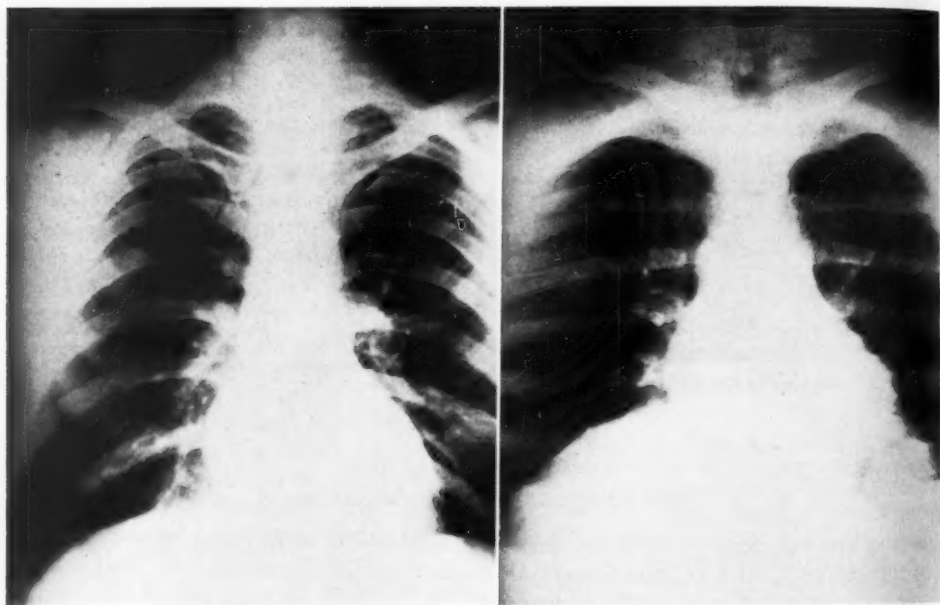


Fig. 1 (left). Postero-anterior view showing "coin" lesion in right upper zone.  
Fig. 2 (right). Lordotic view of lesion.

lem because of the high rate of malignancy. The purpose of this short paper is to record a case of a "coin" lesion of the lung with an unusual pathological basis. As far as could be ascertained, no similar case has been recorded in the literature.

At the Pneumoconiosis Medical and Research Bureau of Northern Rhodesia approximately 40,000 European and African mining recruits and miners are ex-

fection with *S. haematobium* is common in the Central African Bantu, cellular and fibrogenic reaction is minimal and radiological changes are rarely observed (6). The pulmonary pathological findings described by others (2) are unusual. Schistosomal infection in Europeans is much less common and, in view of this and because of the unusual nature of the schistosomal lesion, the case is reported here.

<sup>1</sup> From the Pneumoconiosis Medical and Research Bureau, Kitwe, Northern Rhodesia. Accepted for publication in September 1959.

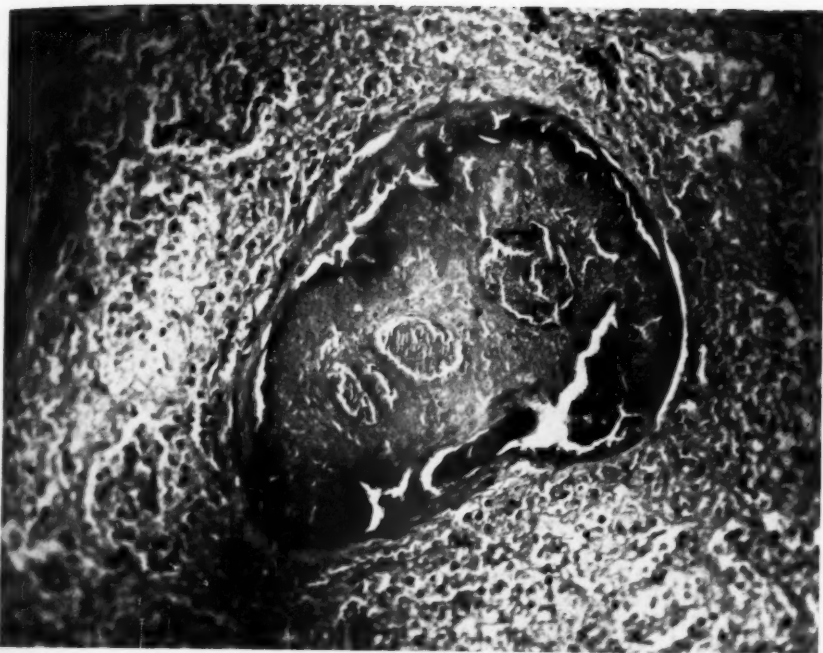


Fig. 3. Schistosome lying intra-arterially, surrounded by infarct. Hematoxylin and eosin.  $\times 120$



Fig. 4. Edge of infarct showing thin layer of granulation tissue separating tumor from normal lung tissue. Hematoxylin and eosin.  $\times 50$

## CASE REPORT

A European miner aged 35 had been clinically and radiologically examined a year previously for employment in a dusty occupation in one of the scheduled copper mines. He was found to be clinically fit, with a normal chest film, and was issued an initial certificate for work in an occupation with a pneumoconiosis hazard. At his annual periodical examination a year later he was found to have a discrete "coin" lesion in the upper lobe of the right lung (Fig. 1). The lordotic view (Fig. 2) shows the lesion more clearly. No symptoms were present and, apart from slight loss of weight, there were no abnormal physical findings. Laboratory investigations were also negative. A presumptive diagnosis of bronchogenic carcinoma was made, and the patient was referred to a thoracic surgeon. Further investigation proved negative, but a malignant lesion was still suspected, and a right upper lobectomy was performed, with an uneventful recovery. On section, the tumor showed no evidence of malignancy. It was found to be composed of a mass of infarcted pulmonary tissue, approximately 14 mm. in diameter, in the center of which thrombosis of the vessels could be seen with a schistosome lying intra-arterially (Fig. 3). Figure 4 is a view of the edge of the tumor showing a thin layer of granulation tissue surrounding the infarct.

## SUMMARY

A "coin" lesion of the lung is recorded with an unusual pathological basis. It consisted of infarcted pulmonary tissue,

with thrombosed vessels and an intra-arterial schistosome.

ACKNOWLEDGMENTS: I am indebted to Mr. A. P. Graham, F.R.C.S., for the tissue from which the photomicrographs were prepared.

P. O. Box 205  
Kitwe, Northern Rhodesia

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## SUMMARIO IN INTERLINGUA

## Lesion Pulmonar "Monetiforme" de Pathologia Inusual

Un lesion "monetiforme" esseva demonstrate in le pulmon de un minero Europee in Sud-Africa. Le patiente esseva asymptomatic, sed ille esseva operate a causa del possibilitate que le umbra repre-

sentava un lesion maligne. Le section revelava un tumor que consisteva de infarcite tissu pulmonar. A su centro, thrombose del vasos esseva visibile, con un schistosoma in location intra-arterial.



## WORK IN PROGRESS

The Use of Varidase During Radiation Therapy of Head and Neck Tumors<sup>1</sup>FRANK GEARING, M.D., PAXTON POWERS, M.D.,  
and GEORGE COOPER, JR., M.D.

The treatment of head and neck tumors by radiation is often complicated by a severe local inflammatory reaction. Swelling, induration, skin erythema, desquamation of oral mucosa, and purulent oral secretions are frequently seen. Lymphatic and venous stasis are prominent features. We have found Varidase<sup>2</sup>—streptokinase-streptodornase—of use in modifying the inflammatory changes.

Streptokinase activates the fibrinolytic system, bringing about the rapid dissolution of clots and fibrinous portions of exudates, while streptodornase liquefies the viscous nucleoproteins of dead cells or pus (1, 2, 3). These proteases have been administered in several clinical conditions, including thrombophlebitis, hematomas and ecchymoses, edema associated with facial and dental surgery, urticaria, contact dermatitis, acute joint inflammation, etc. (4). Because of the beneficial results obtained, Varidase was tried during the irradiation of head and neck tumors complicated by inflammation.

In selecting cases for treatment with Varidase, only those with a full-blown clinical picture, consisting of skin erythema, mucositis, lymphatic stasis, and soft-tissue swelling were considered. This afforded a better opportunity to evaluate effects. Inflammation appeared after a wide tumor dose range (600 to 5,500 r), depending upon whether or not previous radiation therapy had been given and/or the extent of surgical procedures compromising circulation.

Varidase, buccal, one tablet four times daily, was

administered for from four to ten days. The only drug idiosyncrasy observed was increased soreness in the mouth of one patient. Varidase was used in conjunction with general hygienic measures and specific therapeutic agents. Antibiotics were given when indicated.

Effects were graded as 0 to 4+, depending upon subsidence of inflammation and improvement in circulation. Maximum benefit usually occurred within seventy-two hours.

In 14 patients treated to date the effect has been graded as 1+ in 1 patient, 2+ in 3 patients, 3+ in 5 patients, and 4+ in 5 patients. In the patient with a 1+ response an acute psychosis interrupted both the protease and radiation schedules.

In 3 patients oral moniliasis developed during treatment by Varidase and broad-spectrum antibiotics. That the Varidase was responsible seems doubtful.

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<sup>1</sup> From the Department of Radiology, University of Virginia School of Medicine, Charlottesville, Va.

<sup>2</sup> Varidase, brand of streptokinase-streptodornase, supplied by Lederle Laboratories, Pearl River, N. Y.



## NATIONAL COMMITTEE ON RADIATION PROTECTION AND MEASUREMENTS (NCRP)

1. At its meeting in November 1959, the Executive Committee of the NCRP agreed that a statement should be made with regard to the maximum permissible dose from television receivers. Such a statement has been prepared and voted upon by the full committee.

The following position has been adopted by the NCRP:

During the past years members of the NCRP have investigated the emission of x-rays from television receivers. From a genetic point of view even sources of minute radiation are of significance if they affect a large number of people. X-rays emitted by home television sets are, therefore, of interest because of the high percentage of the population involved. In order to insure that the television contribution to the population gonad dose will be only a small fraction of that due to natural background radiation, the NCRP recommends that the exposure dose rate at any readily accessible point 5 cm. from the surface of any home television receiver shall not exceed 0.5 mr per hour under normal operating conditions.

Laboratory and field measurements<sup>1</sup> have shown that with this maximum permissible exposure level the television contribution to the gonad dose at the usual viewing distances will be considerably less than 5 per cent of that due to the average natural background radiation. Most of the present television receivers already meet this requirement with a

high factor of safety. In general, therefore, no changes in shielding of existing sets will be required. However, the recommended limit will insure that future television receivers, operating at higher voltages, will not contribute significantly to the population gonad dose.

2. In its statements of Jan. 8, 1957, and April 15, 1958, the NCRP specified a permissible dose of 10 (N-18 rems) to the skin of the whole body for radiation workers. It has subsequently been realized that the use of the age-proration formula for the skin of the whole body is not practical under some conditions. Therefore, the Committee will discontinue this statement and in its place make the following recommendation:

*Skin of the whole body:* The maximum permissible dose to the skin of the whole body shall not exceed 30 rems per year and the dose in any thirteen consecutive weeks shall not exceed 10 rems.

This statement is essentially the same as in the 1959 ICRP report except that the ICRP specified a 13-week limitation of 8 rems. It is felt that this is unnecessarily low if the annual limit is 30 rems.

3. The above changes will be incorporated in the appropriate reports of the NCRP as the case arises.

<sup>1</sup> Braestrup, C. B., and Mooney, R. T.: X-ray Emission from Television Sets. *Science* **130**: 1071-1074, Oct. 23, 1959.



# EDITORIAL

## Radiation and Borrowed Tissues

The first four papers in this issue of RADIOLOGY, originally presented as a Symposium on Bone Marrow Transplants and General Immunological Problems, at the Forty-fifth Annual Meeting of the Radiological Society of North America, in November 1959, discuss exciting new lines of thought in radiology. They deal with the transplantation of bone marrow and other tissues into individuals who have received lethal or near-lethal doses of radiation. The potential for the saving of human lives from radiation accidents is enough to stimulate us. Beyond this, however, are the implications of therapeutic application associated with radiation given purposefully to near-lethal dosages. This might be expressed as the concept of intentional approach to the brink of radiation disaster followed by heroic rescue through another's tissues. Spectacular medical advances may be achieved by this means. It is possible that a cure for leukemia may be offered by such high-dosage whole-body irradiation, with cell repopulation from a donor's healthy marrow. The treatment of testicular tumors and other malignant neoplasms might be notably improved. A means may be offered for safe transplantation of whole organs from one human being to another.

These hopes are not likely to be achieved easily. The combined efforts of the radiobiologist, geneticist, and immunologist have already paved the way. The reports given here are encouraging, but they also bear witness to the many problems that are yet to be surmounted. We do not know how high the levels of radiation dosage can be pushed, nor what is required for the suppression of such human disease as leukemia. Much remains to be ex-

plored in the immunological phenomena of acceptance or rejection between host and transplant. The late unfavorable sequelae are still an unsolved problem. But these difficulties should not cloud the remarkable achievements already attained. To have successfully effected the removal of a kidney into a new host and to have observed it functioning there—a living chimera—gives high promise for a new era in medicine.

What should be the radiologist's role in these new developments? Clearly, this is not a suitable activity for the casual amateur, but rather for highly integrated units of specialists. We can all be interested in the challenge of this research endeavor and inform ourselves concerning its progress. In the near future, however, few of us are likely to be directly involved in this endeavor, and this is as it should be. A comprehensive mastery of special radiobiological background by the radiologist is required. This must be closely allied to a cooperative effort by radiobiologists, radiological physicists, and other pertinent medical and biological specialists. All of these must be fully informed of the current state of similar work elsewhere. There is no excuse for the same mistakes occurring in several laboratories, for human lives are too much at stake here. Suitable radiation apparatus must be available, and it must be under precise dosimetric control. Even with such an elaborate and pertinent team, ready for operation in favorable surroundings, attitudes of careful objectivity in the selection of patients must be cultivated. Much also remains to be explored at the laboratory level with animals, for there is to be found the basic development of the concepts as well as

new or alternative routes for investigation.

The radiologist who administers whole-body irradiation in amounts likely to be surely lethal unless the patient is rescued by bone-marrow transplantation may have some qualms of conscience. This position is one in which the risks may seem dramatic, but emphasis on that element is inappropriate. Medical choices regarding overtreatment or undertreatment in other situations quite usually include the balance of the patient's health and life. The basic

moral decision is not essentially different in either case.

The radiologist is in an unusually favorable position to watch the course of this scientific adventure. He may have the good fortune to take direct part in some portion of its development. At any rate, he should find it a stimulating source of new interests, worth an optimistic attitude and expanding his contacts into new and exciting directions.

RICHARD H. CHAMBERLAIN, M.D.

## Radiotherapy in Great Britain

A report has just been published by our colleagues overseas reviewing the present status of radiotherapy after ten years of the National Health Service.<sup>1</sup> Although many of the problems inherent in their socialized medical scheme differ from ours, several of the conclusions of this report have poignancy for us as well.

The radiotherapy centers were divided according to size: small (less than 600 new cancer patients yearly), medium (600 to 1,500), and large (more than 1,500). Not unexpectedly, the small centers came in for what would appear to be more than their share of comment:

"Because of the limited staff, experience, clinical and research contacts, physics service, accommodation, and equipment, good quality radiotherapy is far more difficult to provide in the small than in the larger centres. . . .

"Only the most difficult geographical problems . . . would seem to justify the persistence of some of the smaller centres. . . .

"The medium-sized centre treating about 600

new cancer patients per annum is probably the smallest economically sound unit. . . .

"There are still too many little centres dealing inadequately with a small proportion of the total amount of the work done in a specialty where a most expensive range of equipment and ancillary services, which they cannot possibly provide, is necessary for modern and efficient work."

As a practitioner in one of the small centers as defined above, the writer can give these comments a resounding amen. One does not lose stature by securing for his patients a better deal than he can give, by virtue of limited up-to-the-minute knowledge, or limited experience, or limited facilities. As a by-product, he avoids further dilution of certain already uncommon clinical material. Central pooling should lead to quicker answers to pressing problems.

CHRISTIAN V. CIMMINO, M.D.

<sup>1</sup> Radiotherapy After Ten Years of the National Health Service. The Faculty of Radiologists, 47 Lincoln's Inn Fields, London, W.C. 2, England.

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## ANNOUNCEMENTS AND BOOK REVIEWS

### FLORIDA RADIOLOGICAL SOCIETY

The Florida Radiological Society, at a recent meeting, elected John Stewart, M.D., Fort Myers, President; John P. Ferrell, M.D., St. Petersburg, President Elect; Ivan Isaacs, M.D., Jacksonville, Vice President; Richard D. Shapiro, M.D., Miami Beach, Treasurer; Alfred G. Levin, M.D., 837 DuPont Building, Miami, Secretary. J. Maxey Dell, Jr., M.D., is Councilor to the American College of Radiology.

### NASSAU RADIOLOGICAL SOCIETY

Newly elected officers of the Nassau Radiological Society (Nassau County, New York) are: President, Nathaniel Robin, M.D., Garden City; Vice-President, Seymour Wasserman, M.D., Bay Shore; Secretary, Alan E. Baum, M.D., 100 Newbridge Road, Hicksville; Treasurer, Robert Tugenhaft, M.D., Hempstead.

### PACIFIC NORTHWEST RADIOLOGICAL SOCIETY

At the recent annual meeting of the Pacific Northwest Radiological Society, held in Vancouver, B.C., the following officers were elected: President, William Y. Burton, M.D., Portland, Ore.; President-Elect, Homer V. Hartzell, M.D., Seattle, Wash.; First Vice-President, A. Thomas Wiens, M.D., Vancouver, B.C.; Second Vice-President, John W. Loomis, M.D., Portland, Ore.; Secretary-Treasurer, John W. Burke, M.D., 509 Olive Way, Seattle 1, Wash.; Member of Executive Committee, John D. Stevenson, M.D., Vancouver, B.C.

The next annual meeting will be held in Portland, Ore., in May 1961.

### PHILADELPHIA ROENTGEN RAY SOCIETY

The Philadelphia Roentgen Ray Society recently elected to office: Randal A. Boyer, M.D., President; George Wohl, M.D., Vice-President; Robert B. Funch, M.D., Germantown Dispensary and Hospital, Philadelphia 44, Secretary; Luther Brady, M.D., Treasurer; Jack Edeiken, M.D., Counselor at Large.

### COURSE IN SPECIAL RADIATION PROCEDURES IN CANCER QUEENS HOSPITAL CENTER, N.Y.

A one-week intensive course in the use of specialized radiation techniques in the treatment of malignant disease will be given at the Queens Hospital Center, Jamaica, N. Y., beginning Monday, Oct. 17, 1960.

Clinical, operative, and laboratory sessions will be held and will include rotational and arc cobalt teletherapy; interstitial therapy with various radioisotopes; recent technics in the field of isotopes; beta-ray applicators; operative radium technics; modern technics in radium mold fabrication.

The faculty will consist of members of the Radiation Medicine Department, as well as invited guest lecturers.

Further information may be obtained from Dr. Philip J. Kahan, Supervising Medical Superintendent, Queens Hospital Center, 82-68 164th St., Jamaica 32, N. Y.

### AWARD TO DR. W. W. WASSON

W. Walter Wasson, M.D., Denver radiologist and former President of the Radiological Society of North America, received the Norlin Award, highest decoration given by the Associated Alumni of the University of Colorado, at the June 2, 1960, University commencement exercises in Boulder. This award, named for the late President George Norlin of the University of Colorado, is given annually to a person (or persons) who attended the University and later attained great distinction in his field.

The citation reads in part as follows: "Distinguished physician and eminent pioneer in the field of radiology . . . Dr. Wasson has brought great honor to his profession, his State, and his University . . ."

Dr. Wasson received the Gold Medal of the Radiological Society of North America in 1926 and the Gold Medal of the American College of Radiology in 1958.

### UNITED NATIONS SCIENTIFIC COMMITTEE ON EFFECTS OF ATOMIC RADIATION

The United Nations Scientific Committee on the Effects of Atomic Radiation has previously invited Member States to send it data on a wide variety of physical and biological topics. Among these were the following:

1. Physical data relevant to radiation levels and accumulated doses from both natural and man-made sources.

Medical, industrial, and research uses of ionizing radiations and radioactive materials.

Radioactive fall-out.

Measured contamination of air, ground, foodstuffs, and man by  $\text{Sr}^{90}$  and  $\text{Cs}^{137}$ .

Computation of external doses from fall-out deposit, including short-lived isotopes.

Significant disposals of radioactive wastes.

Other significant sources of ionizing radiations.

2. Methods of measurements and radiological standards.



3. Fundamental radiation biology.
4. Somatic effects of ionizing radiation.
5. Genetic effects of ionizing radiation.

There is now brought to the notice of scientists certain areas where an intensification of scientific effort would seem to be most helpful:

*In the biological field:* (i) the mutation-rate, natural and radiation-induced, at specific loci in mammals such as the mouse; (ii) the radiobiological effects of radioactive elements such as  $\text{Sr}^{90}$  in mammals; (iii) the induction of specific new growths such as lymphoma by gamma rays at defined dose rates.

*In the physical field:* (a) levels of  $\text{Sr}^{90}$  in human bones classified by age groups; (b) levels of  $\text{Sr}^{90}$  and  $\text{Cs}^{137}$  in diet; (c) data "linking" rainfall and deposition of  $\text{Sr}^{90}$ .

Scientists who have data to submit on these topics as well as any other facts pertinent to evaluation of effects of radiation, particularly in the low-dose and dose-rate range, are requested to send four copies to Mr. Edward R. Gardner, Director, Office of Special Projects, U. S. Atomic Energy Commission, Washington 25, D. C.

## Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

**MEDULLARY SPONGE KIDNEY: A ROENTGENOLOGIC, CLINICAL, HISTOPATHOLOGIC AND BIOPHYSICAL STUDY.** By TORE EKSTRÖM, BENGT ENGFELDT, CURT LAGERGREN, AND NILS LINDVALL. From the Department of Urology, the Department of Diagnostic Roentgenology, Karolinska Sjukhuset, Stockholm, and the Department of Pathology II, University of Uppsala, Uppsala, Sweden. A monograph of 104 pages, 32 figures. Published by Almqvist & Wiksell, 26 Gamla Brogatan, Stockholm C, Sweden, 1959. Price Sw. kr. 18:— (about \$3.40).

**ENGLISH FOR THE FOREIGN PHYSICIAN.** By JOSÉ MURILO MARTINS, M.D., Assistant Professor of Internal Medicine, University of Ceará, Brazil; Former Resident of Internal Medicine, Kansas University Medical Center, Kansas City, Kans. With a Foreword by E. Grey Dimond, M.D., Professor and Chairman, Department of Medicine, University of Kansas Medical Center, Kansas City, Kans. A monograph of 122 pages, with 18 figures. Published by Charles C Thomas, Springfield, Ill., 1960. Price \$5.75.

**LES PANCRÉATITES CHRONIQUES DE L'ADULTE.** By H. SARLES AND M. MERCADIER, with the col-

laboration of J.-Cl. SARLES, R. MURATORE, AND CL. GUIEN. A volume of 266 pages, with 71 figures. Published by L'Expansion scientifique française, 15, rue St-Benoît, Paris VI, France, 1960. Price 36 NF.

**DIE ASBESTOSE DER LUNGEN: GENESE, KLINIK, RÖNTGENOLOGIE.** By DR. MED. H. BOHLIG, Lüdenscheid/Westf., DR. MED. G. JACOB, Karl-Marx-Stadt, AND DR. MED. H. MÜLLER, Freital b. Dresden. Fortschr. a. d. Geb. d. Röntgenstrahlen, Ergänzungsband 85. A monograph of 166 pages, with 137 illustrations on 97 figures. Published by George Thieme, Herdweg 63, (14a) Stuttgart, Germany, 1960. Distributed in the United States and Canada by the International Medical Book Corporation, New York 16, N.Y. Price DM 66:— (\$15.70); to subscribers to the Fortschritte, DM 59.40 (\$14.15).

## Book Reviews

**THE TREATMENT OF BRONCHIAL NEOPLASMS.** By ROBERT R. SHAW, M.D., AND DONALD L. PAULSON, M.D. With a chapter on Bronchial Adenoma by John Lester Kee, Jr., M.D. A monograph of 136 pages, with numerous figures. Published by Charles C Thomas, Springfield, Ill., 1959. Price \$8.00.

The authors present their philosophy of the treatment of bronchial neoplasms derived from their experience with 1,180 cases of bronchogenic carcinoma. They believe that better results will come not so much through improvement in surgical technic as through better selection of patients for surgical excision to offset the high operative mortality and morbidity.

Irradiation therapy is considered from the standpoint of the clinician, with no attempt to present details of technic. It is felt that in most cases irradiation is to be considered as a palliative agent. The authors state, however, that the results in early cases suggest that this modality may be curative to a greater extent than most physicians realize. Chemotherapy is valuable in the relief of distressing symptoms and in inducing a sense of well being in the patient rather than in lengthening the survival time.

Valuable chapters on the terminal care of the patient and final results are included. A separate chapter deals with bronchial adenoma.

This small volume is a mine of valuable information for surgeons, radiologists, and all clinicians who are concerned with the care of patients with lung cancer.

**ANNUAL REVIEW OF NUCLEAR SCIENCE. VOLUME 9.** Co-editors: EMILIO SEGRÈ, University of California, AND LEONARD I. SCHIFF, Stanford

University. Associate Editors: GERHART FRIEDLANDER, Brookhaven National Laboratory, AND WALTER E. MEYERHOF, Stanford University. A volume of 626 pages, with numerous figures and tables. Published by Annual Reviews, Inc., in co-operation with the National Research Council of the National Academy of Sciences, 1959. On sale by Annual Reviews, Inc., Palo Alto, Calif. Price \$7.00 (U.S.A.); \$7.50 elsewhere.

Most of this Ninth Annual Review of Nuclear Science deals with nuclear physics and will be of little interest to clinical radiologists. An exception is the chapter by Roberts Rugh, entitled "Vertebrate Radiobiology (Embryology)." In this he discusses radiation damage to the embryo and fetus for a variety of experimental animals, correlating such observations with available information on man. In view of the recent concern over the diagnostic use of radiation, particularly in pregnant women, this chapter is well worth reading.

L'ÉPAULE EN PRATIQUE RHUMATOLOGIQUE. By S. DE SÈZE, A. RYCKEWAERT, AND M. MAITRE. Travail du Centre de rhumatologie Viggo-Petersen de l'Hôpital Lariboisière (Paris). A monograph of 170 pages, with 208 figures. Published by Masson & Cie, 120, Blvd. Saint-Germain, Paris, VI<sup>e</sup>, France, 1959. Price 3,800 fr.

This monograph represents a rather thorough coverage of a single painful joint—the shoulder. Anatomic and physiologic data of interest are followed by a very thorough discussion of peritendinitis and other periartritic conditions.

Infectious, rheumatoid, hypertrophic, and neuropathic joint diseases are included. Gout, parasitic diseases, tumors, and other conditions which might conceivably produce shoulder symptoms are also covered.

This is an excellent treatise on a limited topic which may be reviewed profitably by radiologists and rheumatologists. The numerous illustrations are of high quality.

THE HUMAN SPINE IN HEALTH AND DISEASE: ANATOMICOPATHOLOGIC STUDIES. By GEORG SCHMORL, M.D. CLINICORADIOLOGIC ASPECTS. By HERBERT JUNGHAANS, M.D. The first American edition, translated from the fourth German edition, and edited by STEFAN P. WILK, M.D., AND LOWELL S. GOIN, M.D. A volume of 286 pages, with 419 figures. Published by Grune & Stratton, New York, 1959. Price \$21.00.

For many years the classic work on the spine by Schmorl and Junghanns was available only in

German. Now, through the English translation by Drs. Wilk and Goin, we at last are afforded an opportunity to read it in English.

This work is based on the anatomicopathologic studies of Schmorl, who removed many thousands of spines at autopsy and subjected them to the most intense pathologic and radiographic examination. The clinicoradiologic aspects are contributed by Junghanns, who continued to edit succeeding German editions of the work following his colleague's death.

The text covers almost all aspects of the development of the spine and the pathologic lesions which involve the vertebrae and disks. Deformities and physiologic changes are also described. The section devoted to the intervertebral disks is of unusual interest and value. The authors' pioneer studies of these structures have contributed largely to our present knowledge of their physiology and pathology.

The illustrations are superb and bring the text alive. Many of them are radiographs of pathologic specimens and show excellent detail.

This is one of the finest texts devoted to the human spine, and radiologists who do not read German easily are fortunate to have it available in translation. It will be of interest also to workers in other fields of medicine.

STRAHLENBELASTUNG UND STRAHLENSCHUTZ IN DER PÄDIATRISCHEN RÖNTGENDIAGNOSTIK. By PRIV.-DOZ. DR. KURT HARTUNG, Mainz. A monograph of 128 pages, with 26 figures and 97 tables. Published by Georg Thieme, Herdweg 63, (14a) Stuttgart, Germany, 1959. Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 18.60:—(\$4.45).

Although there has been much discussion about protection in diagnostic roentgenology, relatively little of it has concerned children, in whom dose measurements are more difficult than in the adult. This monograph represents a thorough study of the problem in the pediatric group. Clinical measurements on living patients were supplemented by postmortem measurements.

There are several pictures of protection devices, such as gonad shields. An adjustable lead rubber curtain is shown on a fluoroscopic table; this may be moved up and down according to the size of the patient. A wooden table may be placed between the fluoroscopic table and screen to increase focal-skin distance.

These and many other aspects of protection are well presented. The work is recommended for those interested in this field.

## IN MEMORIAM

"Our life is but a little holding, lent to do a mighty labour . . . ." George Meredith



DONALD SMYTHE CHILDS, M.D.

1888-1960

The bleak title above is undoubtedly shocking to those who had to this moment been uninformed. Our loss is sufficiently serious that only straightforward description of the accomplishments of this most unusual person should be recorded. An attempt will be made, nevertheless, to include some of the lesser and lighter things that went on in a life which made Don Childs a man, a physician, and an outstanding radiologist. Don was well known to the majority of American radiologists and most will remember him as one who contributed as much as any individual to

the development of Radiology. His activities were diverse in both public and private life. He was gregarious and out-going—loving his family and enjoying people in all walks of life—young and old. He was more interested in others than in himself. To have known him intimately throughout his life would indeed have been a privilege.

Donald S. Childs was born of Laura Smythe and Henry Ward Childs in Syracuse, N.Y., January 5, 1888. He was educated in the Syracuse elementary and high schools and thence matriculated at Syra-

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cuse University, graduating from the College of Medicine in 1909.

His professional activities, particularly in the field of education and in hospital service, were long, extremely productive, and might well be termed fundamental. In 1914 he became Professor of Radiology in Syracuse University College of Medicine, a position which he continued to hold until 1948, when he was appointed Emeritus Professor of Radiology. In addition, he was Instructor and subsequently Professor of Osteology in the same College for twenty-eight years. He held numerous appointments in various hospitals in Syracuse as radiologist. For years at St. Mary's Maternity Hospital Dr. Childs was not only radiologist but also physician and obstetrician, caring for the patients and staff of the hospital. Actually he continued his radiological activities at St. Mary's for forty years. In addition he was the radiologist for Elmcrest Children's Center and the House of Providence for thirty years.

During World War I he served in the Medical Corps as a Captain. Although he never tended to overemphasize his Army experience, he was extremely proud of his opportunity to serve his country.

Dr. Childs' society affiliations were widespread but he is probably best known through his activities as Secretary-Treasurer of the Radiological Society of North America from 1931 until his death. In 1931, also, he became business manager of RADIOLOGY, the Society's official organ, at a time when its fortunes were at a low ebb. To his wise management was due its continuous growth to the enviable position it holds today. He was a Trustee of the American Board of Radiology from 1940 until 1958 and was President of the Board of Trustees in 1957 and 1958. He was a Fellow of the American College of Radiology and a member of the American Roentgen Ray Society, a loyal member of the American Medical Association, Chairman of the Section of Radiology 1956-1957, and had been a President of the Academy of Medicine in Syracuse. The Gold Medal of the Radiological Society of North America for outstanding contributions to the science of Radiology was awarded to him in 1949. Blue Cross and Blue Shield plans of Syracuse occupied his interest from the time of their inception, and he was a member of the Board of Directors of each until his death. Only a smattering of his educational, professional, and organizational inclination has been indicated, but it suggests the scope of his productive scientific life.

As is often the case, it is the small happenings, the events of apparently minor importance that paint a clearer and more vivid picture of the person under discussion than do the more spectacular things. Don's enthusiasm for baseball was one such. He followed his team each year from Spring practice in Florida throughout the season—in person, when possible—and the members of the team were all his friends. His enthusiasm never flagged from the time they were "dem bums" until they went to Los

Angeles and became "the Angels" and, last Fall, World Champions.

It is less well known that he had a great interest in music. This may well have originated in his college days, when he was working his way through school as a reporter for musical productions, and today he might have been called a music critic. He attended all of the new musical shows opening in Syracuse and reviewed them for the *Post-Standard*. In this way he not only helped to put himself through college and medical school but he became familiar with many of the actors and actresses of the era. To the day of his death he had only to walk into any part of the Palmer House where Ralph Ginsburg was conducting his orchestra, and *Musical Clocks* was played for him.

Throughout his life Dr. Childs' keen understanding of legal matters was recognized, and he was often consulted by attorneys, insurance company executives, and others for his advice. Many years ago he was asked to appear in court to testify and, because it was somewhat inconvenient, tried to change the afternoon hearing to the morning. The attorney was impatient and subpoenaed him. Since his ready assistance in legal matters and his unshakable integrity were well known, the Judge inquired as to the reason for the subpoena, and was informed by Don that he had promised to take his two young sons to the circus that afternoon. Looking at his watch, the Judge asked whether there was still time. The answer was in the affirmative, and the case was dismissed until the following morning. From that day until his death, April 27, 1960, Dr. Childs was never again subpoenaed.

Members of the Radiological Society were well aware of his ability to plan a meeting, but few knew the meticulous care with which he studied each place of meeting to foresee and anticipate every item. He could survey an area, recognize its limitations and advantages, and apply them to the needs of the Society in a manner seldom acquired by a member of the medical profession. Any contemplated place of meeting was visited and, from the moment he arrived until he left, he carried out a strict and thorough inspection of kitchens, meeting rooms, hotel rooms, personnel, etc., to the point where he was able not only to spot the human defects but to recognize any lack of proper mechanical factors. Few physicians have ever attained such perspicacity.

A friendly interest in others earned for Don the love and deep gratitude of those who were the recipients. It is doubtful that anyone will ever know the extent of his benefactions. As his body lay at rest, many an unknown person—a former maid at a hospital, a floor cleaner, a ditch digger—came and paid his respects. On his twenty-fifth anniversary as Secretary-Treasurer of the Radiological Society of North America, when at the Annual Banquet at the Palmer House he received a silver tray inscribed by all of the past Presidents during his regime as Secretary, one of the retired

captains, Frank Messiah, led the ice parade. Frank Messiah and Don Childs were friends over many years, and because their birthdays occurred on approximately the same date, they exchanged telegraphic greetings throughout their active lives. Because of Frank Messiah's admiration for Don, he came out of retirement to captain the ice parade that evening.

Relatively few persons knew that Don Childs was an ardent fisherman and a lover of outdoor life. He spent his summers, or at least as much time as was available to him, in close contact with his family and friends at their summer home "PAOWNYC"<sup>1</sup> on Fourth Lake in the Adirondacks. Here his love of fishing was enjoyed and his culinary attainments were displayed. His popular Saturday night suppers of hamburgers, pancakes, popovers, and other dishes prepared after his own favorite recipes were heartily received. Actually this was only a preparation for extension of these activities to the Century Club of Syracuse and to the Radiological Society of North America.

Throughout his life, his family was foremost in his love and thought. They were held together by a close bond, but never did Don urge any one of them into a field which he felt might be only for self-attainment. It is well known that he constantly carried with him a chain bracelet composed of a collection of small silver disks engraved with each grandchild's name and birthdate.

Donald Childs is survived by his beloved wife, Amy Edwards; his two sons, Dr. Donald S. Childs, Jr., of Rochester, Minnesota, and Eleazer, better known as Lee, of Syracuse, and by nine grandchildren.

To have known Don Childs well for a relatively small segment of his life results in an incomplete understanding of all the great things which he represented. There are no words to describe his contribution to radiology. This was largely through his strong activities in the Radiological Society of North America, the Section of Radiology of the American Medical Association, and the American Board of Radiology. Possibly the most cogent summary of his personal life is found in an editorial in a Syracuse paper:<sup>2</sup> "Don Childs was best known to his many friends for his warm personality, his genial good nature, and his affection for his fine family. He will be sorely missed both professionally and personally." The Radiological Society of North America and all of radiology not only echo this but emphasize it many times over.

LAURENCE L. ROBBINS, M.D.

<sup>1</sup> Pennsylvania, Ontario-Western, New York Central. Mr. O. M. Edwards, Dr. Childs' father-in-law, who invented the Pullman windows and the trap door used on all trains, entertained the railroad officials at his summer home and thus was born the name, Paownyc.

<sup>2</sup> The Post-Standard, Syracuse, N. Y., April 29, 1961.



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JOSEPH CLARK BELL, M.D.

1892-1960

Dr. Joseph Clark Bell died quietly in his sleep in the late afternoon of April 25, 1960, of chronic mitral heart disease, from which he had suffered for a number of years. "Joe" was President of the Radiological Society of North America in 1952. He had previously been President of almost every group to which he belonged, including the Jefferson County Medical Society and the Kentucky Radiological Society.

Joseph Clark Bell was born on August 10, 1892, in Punxsutawney, Pennsylvania. He was raised in the Pacific Northwest, in the State of Oregon, and was graduated in 1917 with an A.B. degree from the University of Oregon. In 1923 he received his M.D. from Harvard University. He interned at the Presbyterian Hospital in New York City and then became one of Dr. Ross Golden's first residents in Radiology at that institution.

Having moved to Louisville in 1925, he shortly became the radiologist for the Norton Memorial Infirmary and also opened a private office. At the time of his death this had expanded to the partnership of Bell, Douglas, Peterson, Blackburn, and Hale.

Dr. Bell had a long and enviable military record, being a Staff Sergeant in the 91st Infantry Division overseas in World War I. He was an active member of the Naval Reserve between the wars, reaching the rank of Lieutenant Commander. In World War II he served as Chief of Radiology at the Percy Jones General Hospital in Battle Creek, Michigan, with the rank of Lieutenant Colonel.

Dr. Bell's principal interest in Radiology was in roentgen diagnosis and he had, for a busy practitioner, numerous publications in this field. He was consultant to the Armed Forces Institute of Pathology and a Professor in the Department of Radiology of the University of Louisville.

He was a man with extremely wide interests, who was always available for civic duties when called

upon. He was a member of the Board of Directors of the Kentucky Blue Shield-Blue Cross, in which he was extremely active until the last. He had been a member of the Board of Chancellors of the American College of Radiology for some years. His circle of friends extended beyond Louisville, throughout the nation and embraced people in all walks of life.

While at the Presbyterian Hospital in New York, Joe met and married Lorraine Seeley. Their family consists of two sons, Nathaniel S. Bell and Joseph C. Bell, Jr., and a daughter, Mrs. Jonathan W. Burr, of Baltimore. There is one grandchild.

With the passing of Dr. Bell, the younger radiologists in particular have lost one of their best friends, for he was alert to the challenge of youth and its new ideas. His high offices gave him many opportunities to advance the cause of the younger men in the national societies and we are most appreciative. We share with his devoted family the grief of his passing.

EVERETT L. PIRKEY, M.D.

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## RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

*Editor's Note:* Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

**RADIOLOGICAL SOCIETY OF NORTH AMERICA.** *Ading Secretary-Treasurer*, Robert P. Barden, M.D., 8835 Germantown Ave., Philadelphia 18, Penna.

**AMERICAN RADIUM SOCIETY.** *Secretary*, Charles C. Stetson, M.D., Englewood Hospital, Englewood, N. J. Next Annual Meeting, Colorado Springs, Colo., May 11-13, 1961.

**AMERICAN ROENTGEN RAY SOCIETY.** *Secretary*, C. Allen Good, M.D., Mayo Clinic, Rochester, Minn.

**AMERICAN COLLEGE OF RADIOLOGY.** *Exec. Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6.

**AMERICAN CLUB OF THERAPEUTIC RADIOLOGISTS.** *Secretary*, Juan A. del Regato, M.D., 2200 North Cascade Ave., Colorado Springs, Colo.

**ASSOCIATION OF UNIVERSITY RADIOLOGISTS.** *Secretary-Treasurer*, Melvin M. Figley, M.D., 7010 51st Ave., N.E., Seattle, Wash.

**SECTION ON RADIOLOGY, A. M. A.** *Secretary*, T. Leucutia, M.D., 10 Peterboro, Detroit 1, Mich.

**SOCIETY OF NUCLEAR MEDICINE.** *Secretary*, Robert W. Lackey, M.D., 452 Metropolitan Bldg., Denver 2, Colo.

**SOCIETY FOR PEDIATRIC RADIOLOGY.** *Secretary-Treasurer*, Richard D. Lester, M.D., 412 Union St. S. E., Minneapolis 14, Minn. Next meeting, Sept. 26, 1960, Atlantic City, N. J.

### Alabama

**ALABAMA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. Garland Wood, Jr., M.D., Medical College of Alabama, Birmingham 3.

### Arizona

**ARIZONA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Don E. Matthiesen, M.D., 926 E. McDowell Rd., Phoenix. Annual meeting with State Medical Association; interim meeting in December.

### Arkansas

**ARKANSAS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. B. Scruggs, M.D., 1700 W. 13th St., Little Rock. Meets quarterly.

### California

**CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY.** *Secretary*, William H. Graham, M.D., 630 E. Santa Clara St., San Jose.

**EAST BAY ROENTGEN SOCIETY.** *Secretary*, Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

**LOS ANGELES RADIOLOGICAL SOCIETY.** *Secretary*, Denis C. Adler, M.D., 2010 Wilshire Blvd., Los Angeles 57. Meets second Wednesday, September, November, March, April, and June, Los Angeles County Medical Association Building.

**NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY.** *Secretary*, Rob H. Kirkpatrick, M.D., 1219 28th St., Sacramento 16. Meets last Monday of each month, September through June.

**PACIFIC ROENTGEN SOCIETY.** *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually at time of California State Medical Association convention.

**RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA.** *Secretary*, Joseph F. Linsman, M.D., 436 N. Roxbury Dr., Beverly Hills.

**REDWOOD EMPIRE RADIOLOGICAL SOCIETY.** *Secretary*, Lee E. Titus, M.D., 164 W. Napa Street, Sonoma, Calif. Meets second Monday every other month.

**SAN DIEGO RADIOLOGICAL SOCIETY.** *Secretary*, Stanley A. Moore, M.D., 2466 First Ave., San Diego 1. Meets first Wednesday of each month.

**SAN FRANCISCO RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Merrell A. Sisson, M.D., 450 Sutter St., San Francisco 8. Meets quarterly, at Grison's Steak House.

**SOUTH BAY RADIOLOGICAL SOCIETY.** *Secretary*, Stanford B. Rossiter, M.D., 1111 University Dr., Menlo Park. Meets second Wednesday every month.

**X-RAY STUDY CLUB OF SAN FRANCISCO.** *Secretary*, John H. Heald, M.D., 450 Sutter St., San Francisco 8. Meets third Thursday at 7:30 P.M., Children's Hospital, September through June.

### Colorado

**COLORADO RADIOLOGICAL SOCIETY.** *Secretary*, Bertram L. Pear, M.D., 3705 E. Colfax Ave., Denver 6. Meets monthly, third Friday, at Denver Athletic Club.

### Connecticut

**CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary-Treasurer*, Ralph J. Littwin, M.D., Bristol Hospital, Bristol. Meets bi-monthly, second Wednesday.

### District of Columbia

**RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY.** *Secretary-Treasurer*, William E. Sheely, M.D., 1746 K St., N.W., Washington 6. Meets third Wednesday, January, March, May, and October, 8:00 P.M., in the Medical Society Library.

### Florida

**FLORIDA RADIOLOGICAL SOCIETY.** *Secretary*, Alfred G. Levin, M.D., 837 DuPont Bldg., Miami.

**FLORIDA WEST COAST RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Joseph C. Rush, M.D., Mease Hospital, Dunedin. Meets quarterly at the Tampa Terrace Hotel.

**GREATER MIAMI RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Donald H. Altman, M.D., 2751 Coral Way, Miami. Meets monthly, third Wednesday, 8:00 P.M., at Jackson Memorial Hospital.

**NORTH FLORIDA RADIOLOGICAL SOCIETY.** *Secretary*, Paul A. Mori, M.D., 800 Miami Road, Jacksonville 7. Meets quarterly, March, June, September, and December.

### Georgia

**ATLANTA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Wilson T. Edenfield, M.D., 1026 Scott Circle, Decatur. Meets second Friday, September to May.

**GEORGIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, George W. Brown, M.D., 317 S. 8th St., Griffin, Ga. Meets in November and at the annual meeting of the State Medical Association.

**RICHMOND COUNTY RADIOLOGICAL SOCIETY.** *Secretary*, Wm. F. Hamilton, Jr., M.D., University Hospital, Augusta. Meets first Thursday of each month.

### Hawaii

**RADIOLOGICAL SOCIETY OF HAWAII.** *Secretary-Treasurer*, Louis L. Buzaid, M.D., The Queen's Hospital, Box 861, Honolulu. Meets third Monday of each month.

### Idaho

**IDAHO STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Claude W. Barrick, M.D., St. Alphonsus Hospital, Boise.

### Illinois

**CHICAGO ROENTGEN SOCIETY.** *Secretary-Treasurer*, William F. Hutson, M.D., 5145 N. California Ave., Chicago 25. Meets at the Sheraton Hotel, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

**ILLINOIS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, George A. Miller, M.D., Carle Hospital Clinic, Urbana. Spring and Fall meetings.

**ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary*, William Meszaros, M.D., 1825 W. Harrison St., Chicago.

### Indiana

**INDIANA ROENTGEN SOCIETY.** *Secretary-Treasurer*, David E. Wheeler, M.D., 1500 North Ritter, Indianapolis. Meets twice a year, first Sunday in May and during fall meeting of State Medical Association.

**TRI-STATE RADIOLOGICAL SOCIETY** (Southern Indiana, Northwestern Kentucky, Southeastern Illinois). *Secretary-Treasurer*, James R. Mathews, M.D., 118 S. E. First St., Evansville, Ind. Meets October, January, March, and May.

### Iowa

**IOWA RADIOLOGICAL SOCIETY.** *Secretary*, James T. McMillan, M.D., 1104 Bankers Trust Bldg., Des Moines. Meets during annual session of State Medical Society, and in the Fall.

### Kansas

**KANSAS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Lewis G. Allen, M.D., 807 Huron Bldg., Kansas City, Kans. Meets in the Spring with the State Medical Society and in the Winter on call.

### Kentucky

**KENTUCKY RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Robert H. Akers, M.D., VA Hospital, Louisville 2. Meets monthly, second Friday, at Seelbach Hotel, Louisville.

### Louisiana

**ORLEANS PARISH RADIOLOGICAL SOCIETY.** *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets second Tuesday of each month.

**RADIOLOGICAL SOCIETY OF LOUISIANA.** *Secretary-Treasurer*, Robyn Hardy, M.D., 4324 Magnolia St., New Orleans 15.

**SHREVEPORT RADIOLOGICAL CLUB.** *Secretary*, W. R. Harwell, M.D., 608 Travis St. Meets monthly September to May, third Wednesday.

### Maine

**MAINE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Albert A. Poulin, M.D., Thayer Hospital, Waterville. Meets in June, October, December, and April.

### Maryland

**MARYLAND RADIOLOGICAL SOCIETY.** *Secretary*, Albert B. Shackman, M.D., 705 Medical Arts Bldg., Baltimore 1.

### Michigan

**DETROIT X-RAY AND RADIUM SOCIETY.** *Secretary-Treasurer*, Kenneth L. Krabbenhoft, M.D., 3835 Brush, Detroit 1. Meets first Thursday, October to May, Wayne County Medical Society rooms.

**UPPER PENINSULA RADIOLOGICAL SOCIETY.** *Secretary*, Arthur Gonty, M.D., Menominee. Meets quarterly.

### Minnesota

**MINNESOTA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Donald H. Peterson, M.D., 25 W. Fourth St., St. Paul 2. Meets Fall, Winter, and Spring.

### Mississippi

**MISSISSIPPI RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Bernard T. Hickman, M.D., University of Mississippi Medical Center, Jackson. Meets monthly, on third Thursday, 6:00 P.M., at Hotel Edwards, Jackson.

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**Missouri**

**GREATER ST. LOUIS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Armand E. Brodeur, M.D., 35 N. Central Ave., Clayton 5, Mo. Meets on fourth Wednesday, October to May.

**RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY.** *Secretary*, Gerhard W. Schottman, M.D., 4400 J. C. Nichols Pkwy., Kansas City, Mo. Meets fourth Friday of each month October through May.

**Montana**

**MONTANA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. K. Boughn, M.D., 35—11th Ave., Helena. Meets annually.

**Nebraska**

**NEBRASKA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Ronald E. Waggener, M.D., Nebraska Methodist Hospital, Omaha. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

**Nevada**

**NEVADA RADIOLOGICAL SOCIETY.** *Corresponding Secretary*, Robert M. Taylor, M.D., 2020 W. Charleston Blvd., Las Vegas. Meets during annual session of State Medical Society.

**New England**

**CONNECTICUT VALLEY RADIOLOGIC SOCIETY.** *Secretary-Treasurer*, Paul J. Kingston, M.D., 114 Woodland St., Hartford, Conn. Meets second Friday of October and April.

**NEW ENGLAND ROENTGEN RAY SOCIETY.** *Secretary*, John E. Gary, M.D., 1180 Beacon St., Brookline 46, Mass. Meets third Friday, October through May, Longwood Towers, Brookline, Mass.

**New Hampshire**

**NEW HAMPSHIRE ROENTGEN RAY SOCIETY.** *Secretary-Treasurer*, Paul Y. Hasserjian, M.D., 1470 Elm St., Manchester. Meets three times a year.

**New Jersey**

**RADIOLOGICAL SOCIETY OF NEW JERSEY.** *Secretary*, Austin J. Tidaback, M.D., 912 Prospect Ave., Plainfield. Annual meeting in Spring, Atlantic City; Fall meeting October or November, Newark.

**New York**

**BROOKLYN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Isadore Katz, M.D., 450 Clarkson Ave., Brooklyn 3. Meets first Thursday of each month, October through May.

**BUFFALO RADIOLOGICAL SOCIETY.** *Secretary*, Kenneth H. Seagrave, M.D., Buffalo Medical Group, 537 Delaware Ave., Buffalo 2. Meets second Monday, October to May.

**CENTRAL NEW YORK RADIOLOGICAL SOCIETY.** *Secretary*, Joseph A. Head, M.D., Hospital of the Good Shepherd, Syracuse University, Syracuse. Meets first Monday, October through May.

**KINGS COUNTY RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, C. P. Naidorf, M.D., 411 Parkside Ave., Brooklyn 26. Meets fourth Thursday, October to April (except December), at 9:00 P.M., Kings County Medical Bldg.

**NASSAU RADIOLOGICAL SOCIETY.** *Secretary*, Alan E. Baum, M.D., 100 Newbridge Road, Hicksville, N. Y. Meets second Tuesday, February, April, June, October, and December.

**NEW YORK ROENTGEN SOCIETY.** *Secretary*, William B. Seaman, M.D., 622 W. 168th St., New York 32, N. Y.

**NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Irving Van Woert, Jr., M.D., Albany Hospital, Albany. Meets in the capital area second Wednesday, October, November, March, and April; annual meeting, May or June.

**RADIOLOGICAL SOCIETY OF STATE OF NEW YORK.** *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meets annually with the State Medical Society.

**ROCHESTER ROENTGEN-RAY SOCIETY.** *Secretary-Treasurer*, Robert H. Greenlaw, M.D., 188 Irvington Road, Rochester 20. Meets last Monday of each month, September through May.

**WESTCHESTER RADIOLOGICAL SOCIETY.** *Secretary*, Richard P. Avonda, M.D., 212 Harwood Bldg., Scarsdale. Meets third Tuesday of January and October and as announced.

**North Carolina**

**RADIOLOGICAL SOCIETY OF NORTH CAROLINA.** *Secretary-Treasurer*, Owen Doyle, M.D., 1015 Professional Village, Greensboro. Meets in spring and fall of each year.

**North Dakota**

**NORTH DAKOTA RADIOLOGICAL SOCIETY.** *Secretary*, Richard F. Raasch, M.D., P.O. Box 990, Dickinson. Meets in the Spring with State Medical Association; in Fall or Winter on call.

**Ohio**

**OHIO STATE RADIOLOGICAL SOCIETY.** *Secretary*, Paul D. Meyer, M.D., 6160 Cherry Hill Dr., Columbus.

**CENTRAL OHIO RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, William B. Schwartz, M.D., 1500 W. Third Ave., Columbus 12. Meets second Thursday, October, November, January, March, and May, 6:30 P.M., Fort Hayes Hotel, Columbus.

**CLEVELAND RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Norman E. Berman, M.D., 14404 S. Park Blvd., Shaker Heights 20. Meets at 7:00 P.M., fourth Monday, October, November, January, February, March, and April, at Tudor Arms Hotel.

**GREATER CINCINNATI RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Stanley J. Lucas, M.D., Provident Bank Bldg., Cincinnati 2. Meets first Monday, September through May, at Cincinnati General Hospital.



**MIAMI VALLEY RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, G. F. Johnson, M.D., 1030 Reibold Bldg., Dayton 2, Ohio. Meets monthly, second Thursday, Miami Valley Hospital, Dayton.

#### Oklahoma

**OKLAHOMA STATE RADIOLOGICAL SOCIETY.** *Secretary*, J. Murphree, M.D., 617 E. Brookfield, Ponca City.

#### Oregon

**OREGON RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Barbara J. Radmore, M.D., 1162 Willamette St., Eugene. Meets monthly, second Wednesday, October to June, University Club, Portland.

#### Pacific Northwest

**PACIFIC NORTHWEST RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, John W. Burkey, M.D., 509 Olive Way, Seattle 1, Wash. Next annual meeting in Portland, Ore., May 1961.

#### Pennsylvania

**PENNSYLVANIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Frederick R. Gilmore, M.D., Clearfield Hospital, Clearfield. Next annual meeting, Bedford Springs Hotel, May 26-27, 1961.

**PHILADELPHIA ROENTGEN RAY SOCIETY.** *Secretary*, Robert B. Funch, M.D., Germantown Hospital, Philadelphia 44. Meets first Thursday of each month at 5:00 P.M., from October to May, in Thompson Hall, College of Physicians.

**PITTSBURGH ROENTGEN SOCIETY.** *Secretary*, Charles N. Chasler, M.D., Elizabeth Steel Magee Hospital, Pittsburgh 13. Meets monthly, second Wednesday, October through June.

#### Rocky Mountain States

**ROCKY MOUNTAIN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, John H. Freed, M.D., 4200 E. Ninth Ave., Denver 20, Colo. Next annual meeting, Aug. 11-13, 1960, Denver Hilton Hotel, Denver.

#### South Carolina

**SOUTH CAROLINA RADIOLOGICAL SOCIETY.** *Secretary*, Wayne Reeser, M.D., 1600 Ninth Ave., Conway. Meets with State Medical Association in May.

#### South Dakota

**RADIOLOGICAL SOCIETY OF SOUTH DAKOTA.** *Secretary-Treasurer*, Donald J. Peik, M.D., 303 S. Minnesota Ave., Sioux Falls. Meets during annual meeting of State Medical Society.

#### The Southeast

**Southern Radiological Conference.** *Secretary-Treasurer*, Marshall Eskridge, M.D., 1252 Springhill Ave., Mobile, Ala.

#### The Southwest

**SOUTHWESTERN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Ralph S. Clayton, M.D., 1501 Arizona Bldg. 2-A, El Paso, Tex. Meets monthly, last Friday, 6:30 P.M., Paso Del Norte Hotel, El Paso.

#### Tennessee

**EAST TENNESSEE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. Marsh Frere, Jr., M.D., 205 Medical Arts Bldg., Knoxville. Meets in September and January, and prior to State Medical Association meeting.

**MEMPHIS ROENTGEN SOCIETY.** *Secretary-Treasurer*, Hollis H. Halford, M.D., Kennedy VA Hospital, Memphis 15. Meets monthly first Monday, John Gaston Hospital.

**TENNESSEE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, James J. Range, M.D., P.O. Box 324, Johnson City. Meets annually with State Medical Association in April.

#### Texas

**CENTRAL TEXAS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Glenn Addison Stokdyk, M.D., VA Center, Temple. Meets monthly, fourth Monday, at Kosel's Cafe, Temple.

**DALLAS-FORT WORTH RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, W. H. Neil, M.D., 1217 W. Cannon St., Fort Worth. Meets monthly, third Monday, 6:30 P.M., at the Greater Fort Worth International Airport.

**HOUSTON RADIOLOGICAL SOCIETY.** *Secretary*, Edward Singleton, M.D., 6621 Fannin St., Houston 25. Meets monthly, last Monday, at Doctors' Club.

**SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY.** *Secretary*, Hugo F. Elmendorf, Jr., M.D., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets at Fort Sam Houston Officers' Club, third Wednesday of each month, 6:30 P.M.

**TEXAS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, R. P. O'Bannon, M.D., 1216 Pennsylvania Ave., Fort Worth 4. Next meeting in Fort Worth, Jan. 20-21, 1961.

#### Utah

**UTAH STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Richard Y. Card, M.D., St. Mark's Hospital, Salt Lake City 3. Meets third Wednesday, January, March, May, September, November.

#### Vermont

**VERMONT RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, John R. Williams, 46 Nichols St., Rutland.

#### Virginia

**VIRGINIA RADIOLOGICAL SOCIETY.** *Secretary*, Frank A. Kearney, 2nd, M.D., 110 S. Curry St., Phoebus.

#### Washington

**WASHINGTON STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Joseph T. Houk, M.D., 14303 Ambaum Blvd., Seattle 66. Meets third Monday of each month, September to April, University of Washington Medical School.

#### West Virginia

**WEST VIRGINIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Karl J. Myers, M.D., Myers Clinic Broadus Hospital, Philippi. Meets with State Medical Society, and as announced.

## Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Joseph F. Wepfer, M.D., 5000 W. Chambers St., Milwaukee 10. Meets fourth Monday, October through May, at the University Club.

SECTION ON RADIOLOGY, STATE MEDICAL SOCIETY OF WISCONSIN. *Secretary*, Abraham Melamed, M.D., 425 E. Wisconsin Ave., Milwaukee 2. Meets in October with State Medical Society.

WISCONSIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Howard G. Bayley, M.D., 124 Winn Terrace, Beaver Dam.

## Puerto Rico

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA. *Secretary-Treasurer*, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, P.R.

## CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS. *Honorary Secretary-Treasurer*, Robert G. Fraser, M.D.; *Associate Honorary Secretary-Treasurer*, Jean-Louis Leger, M.D. *Central Office*, 1555 Summerhill Ave., Montreal 25, Quebec. Meets in January and June.

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTRO-RADIOLOGIE MÉDICALES. *General Secretary*, Louis Ivan Vallée, M.D., Hôpital Saint-Luc, 1058 rue St-Denis, Montreal 18. Meets third Saturday of each month.

L'ASSOCIATION DES RADIOLOGISTES DE LA PROVINCE DE QUÉBEC. ASSOCIATION OF RADIOLOGISTS OF THE PROVINCE OF QUEBEC. *Secretary*, O. Raymond, M.D., 5400 Blvd. Gouin W., Montreal 9. Meets four times a year.

MONTREAL RADIOLOGICAL STUDY CLUB. *Secretary-Treasurer*, Fleming McConnell, M.D., 1650 Cedar Ave., Montreal, Que. Meets first Tuesday evening, October to April.

TORONTO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, L. R. Harnick, M.D., X-Ray Department, Toronto Western Hospital, 399 Bathurst St. Meets second Monday evening, September to May.

## CUBA

SOCIEDAD CUBANA DE RADIOLOGÍA Y FISIOTERAPIA. *Secretary*, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Havana. Meets monthly.

## MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA. *Headquarters*, Calle de Coahuila, Núm. 35, Mexico 7, D. F. *Secretary General*, Dr. Jorge Ceballos Labat. Meets first Monday of each month.

## PANAMA

SOCIEDAD RADIOLÓGICA PANAMEÑA. *Secretary-Editor*, Luis Arrieta Sánchez, M.D., Apartado No. 86, Panama, R. de P.



# ABSTRACTS OF CURRENT LITERATURE

## ROENTGEN DIAGNOSIS

### The Head and Neck

- TAVERAS, JUAN M., AND POSER, CHARLES M. Roentgenologic Aspects of Cerebral Angiography in Children..... 141
- SALTZMAN, GEORG-FREDRIK. Angiographic Demonstration of the Posterior Communicating and Posterior Cerebral Arteries. II. Pathologic Angiography..... 141
- SUSSMAN, BERNARD J., AND FITCH, THOMAS S. P. Thrombolysis with Fibrinolysin in Cerebral Arterial Occlusion: The Role of Angiography..... 142
- SALTZMAN, GEORG-FREDRIK. Circulation Through the Anterior Communicating Artery Studied by Carotid Angiography..... 142
- WIEDENMANN, O., AND HIPPE, E. Abnormal Communications Between the Branches of the Internal Carotid Artery and the Basilar Artery (Carotid-Basilar Anastomosis)..... 142
- SCHMITZ, ALFRED L. Changes in the Ambient Wing Cisterns Secondary to Intracranial Masses..... 143
- KEVILLE, FRANKLIN J., AND WISE, BURTON L. Intracranial Epidermoid and Dermoid Tumors..... 143
- EDEIKEN, JACK, AND NAGLE, WILLIAM. Hyperparathyroidism with Pseudoerosion of the Sella Turcica. Report of Case..... 143
- JACOBSON, GEORGE, AND BLEECKER, H. HARLAN. Pseudosubluxation of the Axis in Children... 143

### The Chest

- TEIXEIRA, JESSE, AND TEIXEIRA, L. C. VIEIRA. Bronchography Without Oil and Iodine—The Use of Barium as a Contrast Medium..... 144
- VANCE, JOHN W., ET AL. The Solitary Circumscribed Pulmonary Lesion Due to Bronchogenic Carcinoma: a 3-Year Follow-up Study of 94 Surgically Treated Patients.... 144
- COLLIER, FRED C., ET AL. Teratoma of the Lung..... 144
- BOYE, ERNST. Progressive Bullous Emphysema: "Vanishing Lung."..... 145
- KOCH, DONALD A. Roentgenologic Considerations of Capillary Bronchiolitis..... 145
- HODGE, JOSEPH, ET AL. Primary Mediastinal Tumors..... 145

### The Heart and Blood Vessels

- KEATS, THEODORE E., AND MARTT, JACK M. Acyanotic Tetralogy of Fallot..... 146
- LYONS, HAROLD A., ET AL. Angiocardiographic Study of Atrial Thrombi with Surgical-Pathological Correlation..... 146
- SCHOBINGER, ROBERT. Transspinous Angiography of the Inferior Vena Cava..... 146

- O'LOUGHLIN, B. J. Caval Contrast Radiography CRITTENDEN, I. HUNTER, ET AL. A Syndrome Featuring Defects of the Heart, Sternum, Diaphragm, and Anterior Abdominal Wall.... 147
- GONDOS, BELA, ET AL. Dissecting Aneurysm of the Aorta. Report of Two Cases Diagnosed by Angiocardiography..... 147
- CASTELLANOS, A., ET AL. Thoracic Aortography Versus Levoangiocardiology..... 147
- TORI, GIULIO, AND GARUSI, GIANFRANCO. Congenital Absence of Right Pulmonary Artery with Patent Ductus Arteriosus and Auricular Septal Defect. Angiocardiographic Diagnosis, 148
- WALDHAUSEN, JOHN A., ET AL. Pulmonic Stenosis Due to Compression of the Pulmonary Artery by an Intrapericardial Tumor... 148
- HODGSON, CORRIN H., ET AL. Hereditary Hemorrhagic Telangiectasia and Pulmonary Arteriovenous Fistula. Survey of a Large Family.. 148
- CURRARINO, GUIDO, ET AL. Abnormal Congenital Fistulous Communications of the Coronary Arteries..... 149
- KAY, JEROME HAROLD, ET AL. Successful Repair of Sinus of Valsalva-Left Atrial Fistula..... 150
- KELLY, PATRICK J., ET AL. The Effect of Arteriovenous Fistulae on the Vascular Pattern of the Femora of Immature Dogs. A Microangiographic Study..... 150
- SANDERS, RICHARD J., AND MORROW, ANDREW G. The Identification and Quantification of Left-to-Right Circulatory Shunts. A New Diagnostic Method Utilizing the Inhalation of a Radioactive Gas, Kr<sup>83</sup>..... 150

### The Digestive System

- TEMPLETON, F. E. Gastrointestinal Radiology.. 151
- KATZ, JOSEPH, AND COHEN, GEORGE. A Preliminary Statistical Survey of Carcinoma of the Oesophagus in the African with Special Reference to Acquired Oesophageal Fistulae. 151
- MULLER, C. J. B. Carcinosarcoma of the Oesophagus..... 151
- LILJEDAHN, S.-O., ET AL. Cineroentgenographic Studies of Gastrointestinal Motility in Healthy Subjects and in Patients with Gastric or Duodenal Ulcer, with Special Reference to Various Methods of Gastrorectomy and the Dumping Syndrome..... 152
- ROWLING, J. THOMPSON. The Prepyloric Septum: A Rare Anomaly..... 152
- SIURALA, M., ET AL. Pernicious Anemia and Gastric Carcinoma..... 153
- KAPO, PETER J. Gastric Pseudodiverticulum Secondary to Pancreatic Pseudocyst..... 153
- FIORITO, EDUARDO S., AND RECALDE CUESTAS, LUIS A. Diagnosis and Treatment of Acute Intestinal Intussusception with Controlled Insufflation of Air..... 153

- MALKASIAN, GEORGE D., JR., ET AL. Volvulus Associated with Pregnancy: A Review and a Report of 3 Cases..... 153
- PONKA, JOSEPH L., ET AL. Coexisting Carcinoma and Diverticula of the Colon. A Review of Three Hundred Fifty-Five Cases of Carcinoma of the Colon..... 154
- EDLING, N. P. G., ET AL. Roentgenologic Findings in Ulcerative Colitis with Malignant Degeneration..... 154
- ROTH, JAMES L. A., ET AL. Toxic Megacolon in Ulcerative Colitis..... 154
- BIRNSTINGL, MARTIN. A Study of Pancreatography..... 155
- VAN DER LINDEN, W., AND HJELMSTEDT, Å. Spontaneous Disappearance of Gallstones.... 155
- RENE, ROBERT M., AND MELLINKOFF, SHERMAN M. Renal Insufficiency After Oral Administration of a Double Dose of a Cholecystographic Medium. Report of Two Cases..... 155
- RIFKIND, BASIL. Death After Cholecystography. 156
- The Diaphragm**
- REED, J. O., AND LANG, E. F. Diaphragmatic Hernia in Infancy..... 156
- MEREDITH, JESSE H., AND BRADSHAW, H. H. Leiomyoma of the Diaphragm..... 156
- GAGLIARDI, RAYMOND A., ET AL. Transient Paradoxical Movement of the Diaphragm..... 157
- The Musculoskeletal System**
- ÖDMAN, PER. Hereditary Enchondral Dysostosis. Twelve Cases in Three Generations Mainly with Peripheral Location..... 157
- ROSENQUIST, R. C., ET AL. Unusual Manifestations of Gout..... 157
- ODELBERG-JOHNSON, OLLE. Osteosclerotic Changes in Myelomatosis. Report of a Case. 158
- SMITH, DAVID W., ET AL. Idiopathic Hypercalcemia. A Case Report with Assays of Vitamin D in the Serum..... 158
- SAMIY, E. Echinococcus Disease of the Calvarium..... 158
- ÅBEL, MARTIN S. Radiologic Aspects of Moderately Severe Cervical Spine Trauma..... 158
- STÖSSEL, H. G., ET AL. Significance of Survey Films (Plain Views) of the Lumbar Spine in Lumbar Intervertebral Disk Prolapse..... 159
- MENSOR, MERRILL C., AND DUVALL, GENE. Absence of Motion at the Fourth and Fifth Lumbar Interspaces in Patients With and Without Low-Back Pain..... 159
- HARTLEY, J. BLAIR. Blind Spots—First Rib Stresses—and the B. I. R. Presidential Address Delivered at the British Institute of Radiology on May 7, 1959..... 160
- STEINBERG, ISRAEL. Huge Osteoma of the Eleventh Left Rib..... 160
- BERNDT, ALBERT L., AND HARTY, MICHAEL. Transchondral Fractures (Osteochondritis Dissecans) of the Talus..... 160
- SCHWARTZ, R. PLATO, AND HEATH, ARTHUR L. Preliminary Findings from a Roentgenographic Study of the Influence of Heel Height and Empirical Shank Curvature on Osteoarticular Relationships in the Normal Female Foot..... 161
- The Spinal Cord**
- KLEFENBERG, GÖSTA, AND SALTZMAN, GEORG-FREDRIK. Gas Myelographic Studies in Syringomyelia..... 161
- LOWREY, JOHN J. Spinal Epidural Hematomas. Experiences with Three Patients..... 161
- Gynecology and Obstetrics**
- RUTLEDGE, FELIX, ET AL. Lymphocysts: A Complication of Radical Pelvic Surgery..... 161
- DONNAN, M. G. F. Radiographic Demonstration of Uterine Developmental Abnormality as a Cause of Abnormal Lie of the Fœtus..... 162
- FRANCIS, H. H. The Etiology, Development, and the Effect upon Pregnancy of Protrusio Acetabuli (Otto Pelvis)..... 162
- The Genitourinary System**
- HAJÓS, E. On the Application of Tomography to Urologic Roentgenology..... 162
- VIAMONTE PUNCET, MANUEL. Nephrocalcinosis: A Clinico-Radiological Study..... 163
- The Adrenals**
- JARVIS, J. LUTHER, AND SEAMAN, WILLIAM B. Idiopathic Adrenal Calcification in Infants and Children..... 163
- Technic**
- FUNCH, ROBERT B. The Dynapulse Method of Ultrashort (Millisecond) Timing and Improved Rapid Impulse Timing in Medical Roentgenography..... 163
- SÖVÉNYI, E. Experiences with Retroperitoneal Air Insufflation (Retropneumoperitoneum)..... 164
- WECHSLER, HERMAN, ET AL. Method for Direct Copy of Radiographs..... 164
- RADIOTHERAPY**
- KAPLAN, HENRY S. New Horizons in Radiotherapy of Malignant Disease..... 164
- DRAKE, ELLERY T., AND DOBBEN, GLEN D. Leiomyosarcoma of the Uterus with Unusual Metastases..... 165
- FREUND, DONALD R., ET AL. Primary Malignant Melanoma of the Vagina..... 165
- ROSENQVIST, HUGO, AND SALTZMAN, GEORG-FREDRIK. Sacrococcygeal and Vertebral Chordomas and Their Treatment..... 165
- WILSON, C. W., ET AL. The Use of the Rad in Clinical Practice: A Symposium at the British Institute of Radiology, November 20, 1958..... 165

## RADIOISOTOPES

- GOOLDEN, A. W. G. Use of Radioactive Iodine in the Diagnosis of Thyroid Disorders. . . . . 166
- SELLER, ROBERT H., ET AL. Use of  $I^{131}$ -Labelled Fat in the Study of Lipid Handling in Patients with Coronary Artery Disease. . . . . 167
- EMMETT, M. L. Surface Back-Scatter for Rectangular Fields in the Quality Range from a Half-Value Layer of 1 mm. of Al to Cobalt 60 Gamma Radiation. . . . . 167
- LAMPERT, P., ET AL. Disseminated Demyelination of the Brain Following  $Co^{60}$  (Gamma) Radiation. . . . . 167
- HICKEY, ROBERT C., ET AL. Cancer Palliation. Extracorporeal Pump Perfusion of Radioactive Isotopes and Nitrogen Mustard as Adjuncts to External Radiation Therapy. . . 167
- NARDI, GEORGE L., ET AL. Liver Blood Flow in Man; Studies Utilizing Radioactive Colloid. I. Normal Values. . . . . 168
- KOENIG, H., AND HELLER, JOHN H. Dynamics of Bone Healing and Its Effect on the Skeletal System in Vivo Using Strontium<sup>90</sup> and Calcium<sup>47</sup>. . . . . 168

## RADIATION EFFECTS

- MURRAY, ROBERT, ET AL. Leukemia in Children Exposed to Ionizing Radiation. . . . . 168

- ROWLAND, R. E., AND MARSHALL, J. H. Radium in Human Bone: The Dose in Microscopic Volumes of Bone. . . . . 169
- ARDRAN, G. M., AND CROOKS, H. E. Observations on the Dose from Dental X-Ray Procedures, with a Note on Radiography of the Nasal Bones. . . . . 169
- CHERRY, C. P., AND GLUCKSMANN, A. Injury and Repair Following Irradiation of Salivary Glands in Male Rats. . . . . 169
- SCHWARTZ, EMANUEL E. Bone Marrow Transplantation and Chemical Protection in the Radiotherapy of Mouse Leukemia (Preliminary Communication). . . . . 169
- ALPEN, E. L., AND BAUM, S. J. Autologous Bone-Marrow Implantation After Fast Neutron Irradiation of Dogs. . . . . 170
- MOLE, R. H. Effects of Dose-Rate and Protraction: A SYMPOSIUM. I. Patterns of Response to Whole-Body Irradiation: The Effect of Dose Intensity and Exposure Time on Duration of Life and Tumour Production. 170
- QUASTLER, H., ET AL. Effects of Dose-Rate and Protraction: A Symposium. II. Adaptation to Continuous Irradiation: Observations on the Rat Intestine. . . . . 170
- WRIGHT, G. PAYLING. Effects of Dose-Rate and Protraction: A Symposium. III. Problems of Injury and Repair in Tissues and Cells: A Review. . . . . 170



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## ROENTGEN DIAGNOSIS

### THE HEAD AND NECK

**Roentgenologic Aspects of Cerebral Angiography in Children.** Juan M. Taveras and Charles M. Poser. *Am. J. Roentgenol.* 82: 371-391, September 1959. (Neurological Institute, 622 W. 168th St., New York 32, N. Y.)

The authors report on 207 cerebral angiograms obtained in 138 children under the age of thirteen. They have previously shown this procedure to be relatively harmless, with only mild and transient complications and less morbidity than is associated with pneumoencephalography (Poser and Taveras: *Pediatrics* 16: 73, 1955. *Abst. in Radiology* 66: 774, 1956). In practically all cases the percutaneous method was used. The technic is essentially the same as in adults. The first six exposures are taken at half-second intervals. Four additional exposures are then made at intervals of one second. This allows visualization of seven seconds of circulation time without increasing the exposure to the patient. If there are clinical signs of increased intracranial pressure, which is known to cause lengthening of the circulation time, the number of exposures at one-second intervals is increased to six.

To avoid distortion of shadows, it has been the authors' custom to take a lateral roentgenogram with the film against the side being injected. In obtaining the anteroposterior view, the roentgen beam is directed in such a way that the superior margin of the orbit and that of the petrous pyramids are superimposed. The tube is angled caudad 12° from the canthomeatal line in adults. In children, slightly less angulation is necessary; an angle of 5° is used routinely, except in children under five years, in whom no angulation is employed. Ten minutes are usually permitted to elapse between any two injections of contrast material. With the use of an automatic injector, 6 c.c. is injected in older children and in adults, and 4 c.c. in children six years of age or younger. With manual injection, the comparable amounts used are 6 c.c. under ten years and 8 c.c. over ten. With the automatic injector the time is set for approximately 1.25 seconds. Routine compression of the internal carotid artery on the opposite side during the injection of contrast substances has been omitted.

Vertebral angiography was carried out in 11 cases. For the anteroposterior projection, a 25° angulation of the tube caudad, relative to the canthomeatal line, is desirable.

*Contralateral filling* of the two anterior cerebral and sometimes of the opposite middle cerebral arteries seems to be more frequent in children—especially younger children—than in adults. This may be related to a lower blood pressure, the smaller size of the capillary bed, and the use of a greater amount of contrast substance than is actually necessary.

In children under ten years of age, some degree of *posterior cerebral artery filling* occurred in about 50 per cent of the examinations, i.e., much more frequently than in adults.

The *average arterial circulation time* was 1.5 seconds. The "capillary phase" is usually not as well defined in children as in adults. The venous phase is about the same as in older patients. The average circulation time (from maximum concentration in the carotid siphon to maximum concentration of the opaque medium in the

parietal veins) is slightly shorter in children than in adults. Any child with a circulation time of 5.5 seconds or over should be considered abnormal. This may be due to increased intracranial pressure or to arterial thrombosis.

The *caliber of the arteries* branching from the internal carotid in children was slightly larger on the average than in adults. This was true particularly of the proximal portion of the anterior and middle cerebral arteries. It was felt that the difference in the size of the vessels was most probably due to some degree of diffuse vascular spasm present in adults during angiography. Children, as well as adults, with bleeding aneurysms show local and diffuse vascular spasm which is not modified by general anesthesia or by the type of contrast substance used.

The *middle cerebral artery* bears a constant relationship to a line drawn from the anterior clinoid process to a point 2 cm. above the lambda. In normal children the middle cerebral artery is always above this line.

Angiography was helpful in obtaining information which tended to elucidate the clinical problem in 58 of 132 patients. The lesions most frequently diagnosed by angiography in adults are supratentorial neoplasm and saccular aneurysm. In children, the proportions are different; venous and arteriovenous angiomas and subdural hematomas are encountered as frequently as neoplasms.

Forty roentgenograms; 3 diagrams; 2 graphs; 3 tables.

JOHN P. FOTOPoulos, M.D.

Northwestern University Medical School

**Angiographic Demonstration of the Posterior Communicating and Posterior Cerebral Arteries. II. Pathologic Angiography.** Georg-Fredrik Saltzman. *Acta radiol.* 52: 114-122, August 1959. (Serafimerlasarettet, Stockholm, Sweden)

In an earlier paper, the author considered the angiographic demonstration of the posterior communicating and posterior cerebral arteries under normal conditions (*Acta radiol.* 52: 1, 1959. *Abst. in Radiology* 74: 863, 1960). The present communication reports a study of a series of patients with intracranial expansive lesions. Two hundred twenty-three carotid angiographies were carried out on the side on which an expansive process was situated or was most advanced. The posterior cerebral artery in this group was visible in 78 cases (35 per cent  $\pm$  3.2 per cent). This incidence of visualization is almost in complete accord with the corresponding figure in a group of normal patients. This would indicate that the posterior cerebral artery is not filled more frequently in tumor cases than in normal subjects. The same may be said of intracranial expansive lesions on the whole.

The vessel was similarly studied in patients with arterial aneurysms and in a small group of cases of arteriovenous aneurysm and of thrombosis in the internal carotid artery system distal to the origin of the posterior communicating artery. The posterior cerebral artery was generally demonstrated less frequently in the presence of aneurysm than in a normal series. Aneurysms of the internal carotid artery at the origin of the posterior communicating artery form an exception to this rule. It is conceivable that the close proximity of the aneurysm may in some way hinder the posterior communicating artery from filling.

With arteriovenous aneurysms, the incidence of filling of the vessel was almost the same as in the normal material. In patients with thrombosis of the internal carotid artery system distal to the origin of the posterior communicating artery, filling of this vessel was obtained much more frequently than in the normal group.

Three tables.

THEODORE E. KEATS, M.D.  
University of Missouri

**Thrombolysis with Fibrinolysin in Cerebral Arterial Occlusion: The Role of Angiography.** Bernard J. Sussman and Thomas S. P. Fitch. *Angiology* 10: 268-282, August (Part 2) 1959. (Montefiore Hospital, New York 67, N. Y.)

Evidence for the efficacy of a thrombolytic agent in cerebral arterial occlusion is difficult to evaluate clinically. Improvement often occurs in untreated cases of cerebral thrombosis. In addition, the signs of an occlusion can be produced by cerebral ischemia of many causes or by hemorrhage. In fact, the actual closure of a vessel may not even be related to the formation of a thrombus within the lumen; obliteration of the vessel lumen can result from extrinsic compression, embolization, atherosclerotic narrowing, or intramural hemorrhage. It is therefore essential that, before a patient is treated and conclusions drawn from his clinical course, the occlusion be established, then localized, and, finally, followed during therapy. This can be done accurately by carotid arteriography. If a patient with hemiplegia has a normal carotid arteriogram, he is best left untreated.

Fibrinolysin was employed in 9 cases of angiographically demonstrated carotid or cerebral vessel occlusion. Favorable results marked by vascular clearing were obtained in 4 cases, 3 of which were embolic in nature. A partially favorable result was attained in 2 cases. In 3 instances, there was no apparent change in follow-up roentgen studies. Postmortem examination disclosed that 1 of these patients suffered a thrombosis of the middle cerebral artery and its branches; this case must be considered a therapeutic failure. In the other 2 patients the exact nature of the occlusion is not known, and atherosclerotic obliteration may have occurred.

Sixteen roentgenograms; 5 photographs; 3 photomicrographs.

**Circulation Through the Anterior Communicating Artery Studied by Carotid Angiography.** Georg-Fredrik Saltzman. *Acta radiol.* 52: 194-208, September 1959. (Serafimerlasarettet, Stockholm, Sweden)

The anterior communicating artery is rarely absent anatomically. With contralateral carotid compression, it is possible angiographically to test whether circulation through this vessel is free. Not infrequently, however, both the pericallosal arteries can be demonstrated at carotid angiography without compression. The author studied the factors which influence this spontaneous passage of contrast medium through the anterior communicating artery in normal and pathological conditions.

In conventional carotid angiograms in the absence of vascular lesions, significant differences in passage through the communicating artery were found on left side injection ( $39.1 \pm 2.1$  per cent) and injection on the right ( $29.5 \pm 2.1$  per cent), in the male ( $39.9 \pm 2.1$  per cent) as compared to the female ( $28.4 \pm 2.1$  per cent),

and with internal carotid injection ( $43.9 \pm 2.0$  per cent) in comparison with common carotid injection ( $21.7 \pm 2.0$  per cent). When extravasation of contrast medium occurred, the incidence of bilateral filling of both anterior cerebral vessels dropped from  $34.7 \pm 1.5$  per cent to  $17.8 \pm 3.8$  per cent. In 14 ( $13.9 \pm 3.4$  per cent) of 101 examinations with extravasation, not even the anterior cerebral artery on the injected side was visible. Blood pressure and prior injection of the external carotid vessel did not significantly influence the passage through the anterior communicating artery, nor was anesthesia or the rate of injection of importance in this respect.

Different contrast media showed a significant difference, but the cause is apparently not related to the concentration. Hypaque 45 per cent produced visualization of the anterior communicating vessel in  $47.3 \pm 4.1$  per cent, and Triurol 50 per cent in  $31.4 \pm 5.0$  per cent. It was noted that passage of contrast material across the midline took place as long as the medium was visible in the carotid siphon in  $43 \pm 5.1$  per cent, but in  $56 \pm 5.1$  per cent the medium could be seen in both pericallosal arteries only while injection was in progress. No significant difference was established between rapid and slow injection.

The author recommends that, for cases in which it is particularly necessary to evaluate passage through the anterior communicating artery, (1) the internal carotid artery should be punctured, (2) rapid serial angiography should be the procedure of preference, and (3) care should be exercised to avoid puncture complications (extravasation).

The incidence of filling of both pericallosal arteries in intracranial expansive processes did not, in general, diverge significantly from the figure obtained in the normal material. The incidence was higher than average in temporal lobe lesions and lower in lesions of the central brain area. There was no difference in passage related to the type of intracranial expansive process.

In arterial aneurysms the incidence of passage was low when the aneurysm was situated at the origin of the posterior communicating artery and the internal carotid artery or in the middle cerebral artery. With aneurysms in the anterior cerebral artery at the origin of the anterior communicating artery, the incidence was higher than in any other part of the analysis. Carotid angiography on the opposite side in these cases revealed incomplete filling of the anterior cerebral artery in nearly one-half of the instances. Hence, if nonfilling of the anterior cerebral artery is noted without puncturing complications, this should be a definite indication for performing a carotid angiography on the opposite side.

Two angiograms; 3 tables.

JOHN A. CAMPBELL, M.D.  
Indiana University Medical Center

**Abnormal Communications Between the Branches of the Internal Carotid Artery and the Basilar Artery (Carotid-Basilar Anastomosis).** O. Wiedenmann and E. Hipp. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 91: 350-365, September 1959. (In German) (Nervenklinik, Universität, München, Germany)

In a review of 7,382 carotid angiograms, the authors found 9 examples of an abnormal communication between a branch of the internal carotid and the basilar artery (carotid-basilar anastomosis). In 6 cases the communication consisted of a primitive trigeminal artery, in 2, a primitive hypoglossal artery, and in 1, a

primitive acoustic artery. The difficulty of demonstrating these carotid-basilar anastomoses radiologically is emphasized. In no case in the present series were there symptoms attributable to the abnormality.

Fourteen roentgenograms, with accompanying diagrams.

**Changes in the Ambient Wing Cisterns Secondary to Intracranial Masses.** Alfred L. Schmitz. *Acta radiol.* 52: 209-216, September 1959. (University of California School of Medicine, San Francisco, Calif.)

The normal ambient wing cisterns are a portion of the subarachnoid space situated around the thalamus. They are perpendicular to the ambient cistern proper, and extend from its anterior superior edge. In life the ambient wing cistern can best be demonstrated by encephalography. On lateral films the two wings are superimposed and appear concave anterosuperiorly. Large ambient wings can occasionally be seen on a frontal view with the central ray approximately perpendicular to the tentorial slit. They extend laterally from the upper anterior portion of the brain stem and outline the pulvinar.

Dislocations of the ventricular system by tumor in the region of the trigone are accompanied by dislocation of the ambient wing cisterns. The direction of displacement reflects the direction of force. In the event that the ventricular system cannot be filled on the diseased side, comparison of the position of the displaced ambient wing cistern with that of the normal wing or ventricle is of great diagnostic import.

The ambient wing cistern may also be displaced by indirect pressure secondary to a herniation of the posterior portion of the temporal lobe through the tentorial slit. These posterior temporal herniations occurred in patients without clinical evidence of increased intracranial pressure.

Thirteen roentgenograms; 2 photographs of anatomical specimens.

EUGENE C. KLATTE, M.D.  
Indiana University Medical Center

**Intracranial Epidermoid and Dermoid Tumors.** Franklin J. Keville and Burton L. Wise. *J. Neurosurg.* 16: 564-569, September, 1959. (University of California School of Medicine, San Francisco, Calif.)

Nineteen cases of intracranial epidermoid and dermoid tumors are reviewed. The average age of the patients was thirty-five years. Eleven were males and 8 females.

Five of the tumors were located in the third ventricle; 5 in the temporal fossa; 3 in the parasagittal region; 3 in the midline posterior fossa; 2 over the convexity of the cerebral hemispheres; and 1 in the cerebellopontine angle. Signs and symptoms varied with the location of the lesion, and were not particularly different from those of other tumors in the same location, except for the relatively long duration (average five years).

Calcification in the lesion was noted on plain roentgenograms of the skull in 7 cases. In 1 patient with an epidermoid in the cerebellopontine angle, erosion of the petrous pyramid was present. Localization of the tumor was accomplished by pneumoencephalography or ventriculography in 9 cases and by carotid angiography in 1 case. In 1 instance a tumor in the posterior fossa that extended into the upper cervical region was diagnosed by myelography.

The results of partial removal of these tumors when they lay within the third ventricle or in the midline of

the posterior fossa were generally poor. Results of treatment of the tumors involving the cerebral hemispheres were better.

Two photographs; 2 tables.

EUGENE A. CORNELIUS, M.D.  
Houston, Texas

**Hyperparathyroidism with Pseudoerosion of the Sella Turcica. Report of Case.** Jack Edeiken and William Nagle. *Arch. Int. Med.* 104: 430-432, September 1959. (Jefferson Medical College Hospital, Philadelphia 7, Penna.)

A case of hyperparathyroidism with osteitis fibrosa cystica is reported. Roentgenograms demonstrated radiolucent defects in the ribs, clavicle, and cervical spine. The bones of the skull showed diffuse demineralization. The sella turcica could not be seen, and it was thought that erosion due to a pituitary adenoma had occurred. Further examination suggested the presence of a mass in the left lower lobe of the thyroid or left parathyroid, and at operation a parathyroid adenoma was removed. It then became apparent that the failure to visualize the bones of the sella was due to their demineralization rather than to erosion from a tumor, as had been suspected. Remineralization followed removal of the parathyroid adenoma. The other skeletal lesions also showed rapid improvement.

Six roentgenograms.

**Pseudosubluxation of the Axis in Children.** George Jacobson and H. Harlan Bleecker. *Am. J. Roentgenol.* 82: 472-481, September 1959. (University of Southern California School of Medicine, Los Angeles 33, Calif.)

The authors describe in detail and illustrate with roentgenograms 4 of 10 cases of anterior dislocations of the axis seen at the Los Angeles County Hospital from 1950 to 1956, in children between the ages of four and six. Clinically there was a history of minor injury with subsequent pain on motion of the head and neck and torticollis. Roentgenograms of the upper cervical spine were judged to be abnormal. After twenty-four to forty-eight hours of immobilization all the patients became asymptomatic.

Lateral roentgenograms of the upper cervical spine revealed either anterior displacement of C2 and C3 and/or angulation at the same level. Since these findings were not noted in normal adults, they were considered pathological until the normal range of motion in children was established as described below.

During infancy and childhood up to the age of ten, flexion and extension are centered at the second and third cervical vertebrae. With flexion of the head and neck, angulation takes place at the level of C2 and C3. Because of the relatively horizontal plane of the articular facets and laxity of the intervertebral ligament, there is a gliding anteroposterior motion between these two vertebrae. Up to 5.0 mm. forward displacement has been noted in a normal child. Posterior displacement of C2 on C3 is noted on hyperextension, but this is less frequent. With extension of the cervical spine, the anterior displacement or angulation was corrected. At about the age of ten, the apex of the flexion curve shifts downward to the C4-C5 or C5-C6 level. In older persons forward gliding of C2 on C3 has not been observed.

In all cases where the axis is displaced anteriorly, or where there is acute angulation at the C2-C3 level, either the head or neck is flexed. Usually the greater

the degree of flexion the greater is the displacement or angulation. Slight flexion of the head may produce an apparent deformity and prolong treatment.

The authors believe that children with injuries to the neck and the above roentgen findings should be treated symptomatically for whatever soft-tissue injury is present, and not for subluxation of the axis.

Twenty-two roentgenograms.

MICHAEL LAZOREK, M.D.  
St. Vincent's Hospital, New York, N.Y.

### THE CHEST

**Bronchography Without Oil and Iodine—The Use of Barium as a Contrast Medium.** Jesse Teixeira and L. C. Vieira Teixeira. *Dis. of Chest* 36: 256-264, September 1959. (Hospital Sanatório Santa Maria, Rio de Janeiro, Brazil)

The chief disadvantage of Lipiodol for bronchography lies in the persistent filling of the alveoli, masking radiologic detail and even in some instances resulting in so-called oil granulomas. The authors used instead a mixture of barium and methylcellulose and believe this to be an excellent bronchographic medium. It has the advantage of demonstrating the whole pulmonary canalicular system, including the delicate peripheral bronchi, without penetrating the alveolar units. In the majority of cases it is completely coughed up by the third day. It is cheap and nontoxic and demonstrates the air channels by coating the mucosa rather than by filling the lumen.

The authors employ a proprietary preparation called Celobar (prepared by Quimica Farmacêutica Maurício Villela, S.A., Rio de Janeiro), consisting of 150 gm. barium sulfate, pur., and 2 gm. methylcellulose. Twenty grams of Celobar is added to 30 ml. of physiologic saline and 20 ml. of this suspension is injected on the side to be opacified first, after which 10 ml. may be introduced on the opposite side.

Excellent results were obtained in 25 patients (200 additional cases, equally successful, are mentioned in an Addendum). The material is readily eliminated by ciliary action and coughing.

Fourteen roentgenograms.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**The Solitary Circumscribed Pulmonary Lesion Due to Bronchogenic Carcinoma: a 3-Year Follow-up Study of 94 Surgically Treated Patients.** John W. Vance, C. Allen Good, Corrin H. Hodgson, John W. Kirklin, and Robert P. Gage. *Dis. of Chest* 36: 231-237, September 1959. (Mayo Clinic, Rochester, Minn.)

Ninety-four patients with single circumscribed pulmonary carcinomatous lesions, proved pathologically, were studied. The cases included only those in which the lesion was situated in the substance of the lung, was rounded, and had a fairly well defined border. In none were there peripheral obstructive changes, central cavitation, pleural effusion, or calcification. Fifty-two of the lesions exceeded 4.0 cm. in diameter; 21 measured 3.1 to 4.0 cm., 16 were 2.1 to 3 cm., and 5 were 2 cm. or less. No lesion less than 1.0 cm. in diameter was treated by resection.

Seventy-seven of the 94 patients had cytologic examination of either sputum or bronchial washings. In 31 (40 per cent) the examination was positive for cancer cells. Bronchoscopy was done in 94, but in only 7 (10

per cent) was a positive tissue diagnosis made. Although clinically all the patients were considered operable, 9 were found to be inoperable, usually because of extensive mediastinal metastases.

The overall three-year survival rate was 36.6 per cent. The three-year survival rate for those with excision of all apparent carcinoma was 44.7 per cent. This figure is almost the same as was obtained by Kirklin *et al.* (*Surg., Gynec. & Obst.* 100: 429, 1955) from the same institution following curvative resection for bronchogenic carcinoma, regardless of whether or not it appeared on the roentgenogram as a solitary nodule. The absence of involvement of lymph nodes did not appear to alter the prognosis, which is explained on the assumption that the distant spread of solitary lesions occurs more by vascular pathways than by lymphatics. There was no significant difference in survival between those undergoing pneumonectomy and those with lobectomy. The survival rate for asymptomatic patients was 15 per cent higher than for those with thoracic symptoms. Fifty-nine of the 94 had symptoms. Seventeen complained of hemoptysis. Of these, 4 had lesions less than 4.0 cm. in diameter. Six had symptoms which were attributed to pulmonary osteoarthropathy; in 4 of these bone symptoms were the only complaint. Ten of the 35 asymptomatic cases were discovered by mobile unit survey-type roentgenograms.

Four tables. MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Teratoma of the Lung.** Fred C. Collier, Edmund A. Dowling, Dwight Plott, and Harold Schneider. *Arch. Path.* 68: 138-142, August 1959. (University of Alabama Medical Center, Birmingham 3, Ala.)

Intrathoracic teratomas are unusual, and an intrapulmonary teratoma is one of the rarities of medicine. The authors report a case of benign teratoma arising in the left upper lobe of the lung in a 46-year-old Negro woman, and review 11 other cases from the literature.

The patient had been subject to recurrent hemoptysis for fifteen to twenty years with attacks of increasing severity in recent years. Blood loss from the last bout of hemoptysis, which led to hospital admission, necessitated replacement transfusion. Between episodes the patient had been relatively asymptomatic except for a mild chronic productive cough, increased susceptibility to upper respiratory infections, and slight dyspnea on exertion.

Bronchoscopy revealed a considerable amount of fresh blood coming from the left upper lobe orifice. Roentgen examination showed an ovoid, air-containing mass, 9 cm. in greatest diameter, in the anteromedial left upper chest. The mass was surrounded by air-containing lung on all sides except for its medial and inferior margins. The medial margin blended with the mediastinum and displaced the left main bronchus and lower trachea slightly toward the right. The inferior margin was limited by focal minimal thickening of the major fissure. Within the cystic mass was a large solid ball, filling the greater part of the cavity and appearing to lie almost free within the cavity. Review of previous films, taken elsewhere, disclosed no change in the lesion over a three-year period. The patient had been aware of abnormal radiographic chest findings for at least ten years. Radiologic diagnoses considered were (1) dermoid cyst communicating with a bronchus; (2) bronchogenic cyst, (3) bronchial adenoma with obstruction and secondary cyst formation.



Two and a half hours after left upper lobectomy, a left hemothorax made a second thoracotomy necessary, and at this time a small bronchial vein and various areas of denuded pleura were ligated. Twenty-six hours postoperatively, supraventricular tachycardia developed, progressing to ventricular fibrillation and death. The pathologic diagnosis was benign cystic teratoma.

Six figures, including 2 roentgenograms.

**Progressive Bullous Emphysema: "Vanishing Lung."** Ernst Boye. *Acta med. scandinav.* 164: 167-174, 1959. (Aarhus Amtssygehus, University of Aarhus, Denmark)

The most common result of chronic bronchopulmonary disease, such as chronic suppurative conditions, pneumoconiosis, and sarcoidosis, is a change in the lungs of a proliferative and fibrotic character, giving a typical roentgen appearance with an increase in the reticular pattern or diffuse nodular infiltrations (in addition to the changes which may be attributed to the original disease). Bullous emphysema, a diffuse disease of the lung with multiple air cavities, produces an entirely different roentgen picture. Here atrophic changes so predominate that they have given rise to the term "vanishing lung."

Bullous emphysema is often symptomless in the early stages and may be discovered quite accidentally on roentgen examination. In the interpretation of the roentgenograms, the first impression may be unilateral pneumothorax or a large lung cyst. Over a large field comprising one or more lobes, the pulmonary markings may be sparse with very fine shadows of vessels, or they may be completely absent. In unilateral cases, the contrast between the two lungs in vascular markings and filling of the vessels is striking; the pulmonary artery is of smaller diameter on the affected side. The costophrenic sulci are free, and the mediastinum is not displaced. Hilar shadows are often absent. In unilateral "vanishing lung," the heart shadow is normal; with bilateral involvement, there may be slight prominence of the pulmonary arch. In advanced stages, the form of the heart resembles that observed in cor pulmonale. In some instances bronchography has shown perfectly normal filling; in others only the bronchi in the hilar region were demonstrated. Bullous emphysema must be differentiated from tuberculous cavities; cysts (there may be a fluid level in a cyst, and the cyst walls are sharply defined as distinct from the fine demarcations of the bullae); pneumothorax; senile emphysema; and from bronchial asthma with emphysema.

Four cases of progressive bullous emphysema are reported. In at least 2 of these, the disease developed into the condition termed "vanishing lung." The author believes that the administration of antibiotics may be a contributing factor in the increasing frequency of bullous emphysema in recent years and advises against their injudicious use in acute bronchopulmonary infections.

Four roentgenograms.

**Roentgenologic Considerations of Capillary Bronchiolitis.** Donald A. Koch. *Am. J. Roentgenol.* 82: 433-436, September 1959. (310 E. Water St., Port Huron, Mich.)

Capillary bronchiolitis is an acute clinical syndrome characterized by respiratory distress and emphysema

developing in an acute respiratory infection in infants. It occurs most commonly during the first six months of life and is rare after the age of two.

The disease is ushered in by a few days of illness with an upper respiratory infection with mild constitutional symptoms, following which there is an acute clinical change characterized by severe respiratory distress with labored breathing and possibly cyanosis. The temperature is usually less than 100° F. The chest appears overexpanded and there is obvious overactivity of the respiratory muscles. There may be diffuse râles and rhonchi. The breath sounds are diminished. The pulse rate is rapid. No specific organism or causative agent has been identified so that sputum samples are of little diagnostic value.

Radiographically, the lung fields are hyperaerated with increased radiolucency and depression of the diaphragmatic leaves. The vascular shadows appear stretched and the costophrenic angles are of diminished acuity. The heart size is reduced, particularly with expiration. In the lateral view, the surface of the diaphragm is depressed in the posterior half of the chest, which is often a reversal of normal convexity. The anteroposterior diameter of the chest is increased. Anteroposterior and lateral projections of the chest taken in inspiration and expiration are recommended to show these features to the best advantage.

Four roentgenograms; 1 photomicrograph.

JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Primary Mediastinal Tumors.** Joseph Hodge, Gonzales Aponte, and Edward McLaughlin. *J. Thoracic Surg.* 37: 730-744, June 1959. (Hodge Clinic, 3 Catawba St., Spartanburg, S.C.)

Seventy-four unselected cases of mediastinal tumor were collected from the records, 1942-1956, of the Departments of Surgery and Oncology of the Jefferson Medical College and Hospital (Philadelphia, Penna.). The authors review the 42 cases in which the tumor was primary in the mediastinum and classify them on the basis of pathologic types in specific anatomic locations. There were 18 thymomas (4 benign, 14 malignant); 11 neurogenic tumors (10 benign, 1 malignant); 8 teratomas and dermoid cysts (benign 2 each; malignant 2 each); 5 incidental tumors (2 bronchial cysts, 1 hamartoma, 1 lipoma, 1 pericardial cyst).

The characteristic clinical, pathologic, and roentgenologic features of the different types of tumor are described. The variety of malignant thymomas and the association of myasthenia gravis with benign thymomas are emphasized.

The roentgen demonstration of a posterior mediastinal tumor favors a diagnosis of a neurogenic neoplasm; the presence of cartilage, bone, teeth, etc., is indicative of teratoid tumor. Lipoma should be considered when one finds an hourglass type of opacity in the neck or chest wall continuous with an intrathoracic mass. A hamartoma may be suspected when roentgenograms show a dense mediastinal mass surrounded by normal pulmonary tissue and exhibiting sharp lobulated borders with areas of calcification.

Thoracotomy with excision of the mediastinal tumor was successfully performed in 36 patients; a biopsy of a supraclavicular node was carried out in 1; the remaining 5 patients were not operated upon.

Five roentgenograms; 5 photomicrographs; 4 photographs; 5 tables.



## THE HEART AND BLOOD VESSELS

**Acyanotic Tetralogy of Fallot.** Theodore E. Keats and Jack M. Martt. *Am. J. Roentgenol.* 82: 417-422, September 1959. (University of Missouri School of Medicine, Columbia, Mo.)

This paper reports 4 cases of tetralogy of Fallot. Each of the patients was acyanotic and each exhibited unusual roentgenographic features, illustrating the variable manifestations of this type of congenital heart disease.

Patients with tetralogy of Fallot may be acyanotic (1) if there is a mild or moderate pulmonic stenosis and a small or moderate-sized ventricular septal defect; (2) if there is a dominant ventricular septal defect with a mild infundibular stenosis which permits a left-to-right shunt at the ventricular level, increasing the pulmonary blood flow; (3) if there is dominant pulmonic stenosis. With right ventricular outflow obstruction and a small ventricular septal defect, a right-to-left shunt results but is limited by the size of the defect. The incidence of acyanotic tetralogy is estimated to be 10 per cent.

Physiologically the degree of pulmonic stenosis and the size of the ventricular septal defect are variable combinations, accounting for the diverse clinical and radiological picture.

In 2 of the cases reported, the radiographic features indicated an isolated interventricular septal defect. Catheterization showed a substantial left-to-right shunt at the ventricular level. A pressure gradient across the pulmonic valve confirmed the presence of the stenotic lesion. In these cases, the ventricular septal defect overbalanced the pulmonic stenosis so that minimal or no right-to-left shunt resulted. This accounts for the lack of cyanosis. In the other 2 cases there was no demonstrable left-to-right shunt, indicating that the pulmonic stenosis was either of a higher degree or the ventricular septal defect was small. In this circumstance, it is reasoned that the septal defect does not permit a sufficient volume of blood shunting from the right to the left side to produce clinical cyanosis. This condition is termed a "balanced shunt." In the 2 cases demonstrating this pathophysiology, the radiographic features were more compatible with pulmonic stenosis.

These concepts are important, since tetralogy of Fallot must now be considered in the differential diagnosis of acyanotic congenital heart disease.

Ten roentgenograms; 1 table.

JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Angiocardiographic Study of Atrial Thrombi with Surgical-Pathological Correlation.** Harold A. Lyons, Murray Strober, John S. McPetridge, and Colin G. Caro. *J.A.M.A.* 170: 1288-1293, July 11, 1959. (450 Clarkson Ave., Brooklyn 3, N. Y.)

The incidence of atrial thrombi in mitral heart disease has been shown by various observers to be higher than in routine postmortem series. In the authors' angiocardiographic studies on 26 consecutive patients with rheumatic mitral disease 10 were found to have thrombi, confirmed either by surgery or autopsy in 8.

The basis for the angiographic diagnosis of atrial thrombi is a persistent area of poor opacification with ill defined margin and irregular shape. Myxomas and ball-valve thrombi have well delineated margins about the area of nonopacification. Myxomas are usually

attached to the atrial septal wall, whereas thrombi are usually attached to the posterior atrial wall. The authors used 3 doses of opaque medium for a complete angiogram. Views were obtained in the postero-anterior and left anterior oblique position for each patient.

The incidence of thrombi in this series is 36 per cent, comparing favorably with the incidence recorded in postmortem studies. As an aid to the evaluation for mitral valvulotomy, angiography provides important and accurate information. In 5 of the cases reported successful surgical correction was possible after the diagnosis of atrial thrombi by opaque studies.

Six roentgenograms; 6 diagrams; 1 table.

D. D. ROSENFELD, M.D.  
Los Angeles, Calif.

**Transspinosus Angiography of the Inferior Vena Cava.** Robert Schobinger. *Angiology* 10: 144-147, June 1959. (130 W. Kingsbridge Rd., Bronx 68, N. Y.)

A technically convenient approach for the roentgen demonstration of the inferior vena cava and its major distal tributaries is presented. The procedure can be carried out rapidly under local anesthesia and requires for its execution only a few simple instruments, all readily available at any hospital. Basically, it follows principles previously outlined for intraosseous venography at various other anatomical levels (see, e.g., *Angiology* 8: 428, 1957. *Abst. in Radiology* 71: 277, 1958). Roentgenographic visualization of the inferior vena cava can be accomplished by injecting contrast medium (Hypaque) at various levels; the best sites for this purpose are the distal two or three lumbar spinous processes and the upper portion of the midsacral spine. Representative normal angiograms of the inferior vena cava are reproduced.

Better than average opacification of the inferior vena cava was attained in all patients with obstructive disorders of the spinal canal if the injection was made below the site of the spinal lesion (spinal cord tumors, metastatic carcinoma, herniated intervertebral disk syndromes). Conversely, the inferior vena cava could not be opacified in 5 patients with cirrhosis of the liver associated with ascites. In these cases there seemingly existed an increased circulation within the epidural veins as compared with that in normal persons; the full physiopathologic significance and clinical implications of this observation must await the accumulation of additional data.

Concomitant inferior vena caval angiography and excretory urography can easily be performed, by two separate injections, the second being carried out after an interval of ten to fifteen minutes.

Four roentgenograms; 1 drawing.

**Caval Contrast Radiography.** B. J. O'Loughlin. *Arch. Int. Med.* 104: 402-405, September 1959. (University of California Medical Center, Los Angeles 24, Calif.)

Roentgen visualization of the inferior vena cava has been found advantageous in many instances of partial or complete occlusion, as by metastatic tumor, growing thrombi, or benign compression. Indications for surgery may depend upon knowledge of the condition of the vessel and the immediately adjacent areas obtainable by contrast radiography.

In the technic described by the author, the patient is prepared as for intravenous urography, the femoral vein

is punctured enough to be made (3) pine. A lateral view. By this demonstr shown. Eight

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is punctured percutaneously, and after withdrawal of enough venous blood to assure a good tap the injection is made (35 per cent iodopyracet) with the patient supine. A film is obtained, the patient is rolled into a lateral position, and the injection is repeated for a lateral view.

By this means not only has the normal vena cava been demonstrated, but many pathological entities have been shown.

Eight roentgenograms.

**A Syndrome Featuring Defects of the Heart, Sternum, Diaphragm, and Anterior Abdominal Wall.** I. Hunter Crittenden, Forrest H. Adams, and Donald G. Mulder. *Circulation* 20: 396-404, September 1959. (University of California, Los Angeles, Calif.)

What is believed to be a distinct syndrome is described by the authors and illustrated by 3 case reports from their own experience. It comprises midline defects in the thoraco-abdominal wall (mesodermal), with diastasis recti, umbilical hernia, and deficiency of the sternum, as well as dextrocardia and dextroversion of the heart, and other cardiac anomalies, of which ventricular septal defects are the most consistent. Formerly such cases have been classified as a form of ectopia cordis.

Plain films demonstrate the dextrocardia and usually increased lung vascularity because of the left-to-right shunt through the ventricular septal defect often present. Angiocardiology and/or catheterization show the position of the ventricles and the septal defect. The various defects in the anterior body wall are easily diagnosed by physical examination.

Seventeen roentgenograms; 1 photograph.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**Dissecting Aneurysm of the Aorta. Report of Two Cases Diagnosed by Angiocardiology.** Bela Gondos, Charles H. Hunter, and Nina Braunwald. *New England J. Med.* 261: 535-539, Sept. 10, 1959. (District of Columbia General Hospital, Washington, D. C.)

The early diagnosis of dissecting aneurysm of the aorta is now of practical importance because of the possibility of surgical intervention. The aneurysm is usually preceded by hypertension and the most important finding is degeneration of the media. There is a transverse tear in the intima usually just above the aortic valve or in the area of the left subclavian artery, and the dissection occurs in the media and extends distally. The patient experiences an agonizing thoracic and abdominal pain, and, depending upon the interference with the blood supply, many different symptoms may ensue. The differential diagnosis includes myocardial infarction, pulmonary embolism, spontaneous pneumothorax, and various abdominal conditions.

Routine roentgenography usually shows evidence of hypertensive cardiovascular disease manifested by enlargement of the heart and elongation and dilatation of the aorta. The widening of the aortic wall is not ordinarily demonstrable, but if films are available from before the dissection an increase in the aortic width may be seen. Occasionally, intimal calcification will mark the inner wall of the aorta and the distance between this and the outer contour will give its width. The normal thickness is 1.5 to 2.5 mm. A width of approximately 1.0 cm. suggests a dissection.

Angiocardiology can provide a positive diagnosis.

Two abnormalities may be noted: an irregular narrowing of the main aortic channel and an increase in distance between this and the external wall of the aorta. Less commonly, the false channel is demonstrated by the opaque material.

Two cases are reported in which angiocardiology was performed. In the first instance the aortic lumen was smooth and a soft-tissue shadow approximately 1.0 cm. in width was noted parallel and adjacent to the opaque column in the descending aorta. This was confirmed as a dissecting aneurysm at subsequent surgery. In the second case the aortic lumen was markedly narrowed starting at the brachiocephalic level and descending to the diaphragm. The wall of the aorta, represented by a less dense shadow than the column of opaque material, was thought to be obviously thickened and was considered to represent a dissecting aneurysm. Surgery was not done and no confirmation was obtained. A later roentgenogram revealed a decrease in the width of the aortic shadow and it was believed that this self cure was caused by the dissected false channel having re-entered the lumen at a lower level.

The rationale of surgery is to prevent ultimate rupture of the outer wall. This is done by decompressing the dissected portion of the aorta by creating an artificial re-entry channel. De Bakey and his associates have devised an operation whereby a window is cut in the proximal end of the aorta and the intima and adventitia are sewed together distally, thus closing off the outer dissected passage.

Five roentgenograms.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Thoracic Aortography Versus Levoangiocardiology.** A. Castellanos, Otto Garcia, Eloina Gonzalez, and Raul Pereiras. *Am. J. Roentgenol.* 82: 403-416, September 1959. (23 No. 1,107, Vedado, Habana, Cuba)

The term "dextro-angiocardiology" refers to the injection of radiopaque material *via* a peripheral vein, for visualization of the right chambers of the heart and the pulmonary artery and its branches. Leaving these vessels, the radiopaque substance is distributed throughout the pulmonary network, and later returns through the pulmonary vein to the left chambers of the heart, the aorta, and its branches. This second phase is called the "levo-angiocardiology."

Although in some congenital or acquired lesions of the aorta levoangiocardiology yields sufficient anatomic information, in other cases thoracic aortography will be necessary. If the aorta arises from the left ventricle, it has less radiodensity in the levo-angiocardiology than the pulmonary artery, because of dilution of the contrast material with blood. Selective angiocardiology, with injection directly into a heart chamber will improve the density. With a left-to-right shunt through a ventricular septal defect, some contrast medium passes into the right heart and the pulmonary artery, resulting in a lesser opacification of the aorta. In cases in which the aorta overrides the interventricular septum or when it arises completely from the right ventricle, its opacification will be very intense in the dextro-angiocardiology. With direct aortic injection, either by the retrograde method or by a catheter introduced into a peripheral artery up to the aortic arch, the density of the aorta and its branches may be so marked as to render possible its distinction from the right and left

cardiac chambers. For this reason, in many cases thoracic aortography provides anatomic details that can hardly be obtained on the levo-angiocardigram.

For *thoracic aortography*, the authors prefer to use the left humeral artery or the left common carotid artery, the former in infants of less than a year. The most advantageous positions for the diagnosis of patent ductus arteriosus and coarctation of the aorta are the left anterior oblique and the lateral. In the frontal position a left subclavian artery arising directly from the aorta to the left side of the midline can best be diagnosed. The frontal and lateral positions are also useful in the differential diagnosis of: aneurysm of the aortic arch and descending aorta; mediastinal tumors; aneurysms of the sinuses of Valsalva; and incompetency or insufficiency of the aortic valves. Cinefluorography is the ideal method for thoracic aortography, but a rapid film-changer making possible four to six exposures per second is usually adequate.

For *levo-angiocardiology*, to obtain good opacification of the left heart chambers and aorta, the contrast medium should be injected within one second, and should be adequate in amount and concentration. The amount should be at least 1.5 c.c. per kilogram of body weight per second. A concentration of 70 per cent is preferred, but with the disodic triiodo compounds the ideal is 90 per cent. In patients over six to eight years old, the use of a seriograph with a selector is recommended. Two or three roentgenograms only are made in the dextro phase, with four or six rapid exposures per second in the levo phase, according to the need.

This paper is based largely on the use of intravenous angiocardiology and thoracic aortography in a children's hospital, and many cardiovascular anomalies are discussed. Excellent illustrations and diagrams of the findings are provided. The interested reader is referred to the original paper for study.

The authors conclude that the indications for thoracic aortography include two groups of cases: those requiring the use of levo-angiocardiology and congenital or acquired lesions which can be diagnosed only from the aortogram. The procedure is of greatest value in coarctation of the aorta, yielding considerably more information than can be obtained through levo-angiocardiology, especially in infants.

Eighteen roentgenograms; 2 tables.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

**Congenital Absence of Right Pulmonary Artery with Patent Ductus Arteriosus and Auricular Septal Defect. Angiocardigraphic Diagnosis.** Giulio Tori and Gianfranco Garusi. *Radiol. clin.* 28: 228-250, July 1959. (In English) (Radiology Institute of Bologna University, Bologna, Italy)

Congenital absence of a pulmonary artery is of much more frequent occurrence than was thought in the past. To the present time probably 80 cases have been published in the world literature. The anomaly may appear by itself or in association with other defects, as patent ductus arteriosus, coarctation of the aorta, or tetralogy of Fallot. The authors report a case of absence of the right pulmonary artery with a patent ductus and a probable interatrial septal defect.

On the plain postero-anterior film, absence of a pulmonary artery may be suspected from increased radiolucency of the lung on the side of the anomaly and decreased vascularity as compared to the opposite side.

The hemithorax also appears smaller, the ribs are closer to one another, and the diaphragm is elevated. The heart may be displaced toward the affected side.

Electrocardiograms may be normal or may indicate hypertrophy of the right ventricle, especially in the presence of an associated tetralogy of Fallot.

Few cardiac catheterization studies have been done. In cases with multiple anomalies increased right ventricular pressures have been found.

Angiocardiology offers the best means of obtaining a diagnosis and ascertaining the presence of associated cardiovascular defects. The majority of the more recently reported cases have been diagnosed by this means.

Many authors have observed good secondary compensatory circulation to the affected lung. Blalock and others have reported cases with a large vessel arising from the subclavian artery to supply the left lung. In other instances the supply has been maintained by a large arterial branch arising from the ascending aorta. In one case of absence of the left pulmonary artery a branch from the right pulmonary served this purpose.

Respiratory function studies have shown the vital capacity of the lung on the affected side to be reduced.

In the authors' case, the symptoms were not such as to allow an exact clinical diagnosis, and the conventional roentgenogram offered only an orientation due to the higher transparency of the right hemithorax and the corresponding fine hilar shadow. It remained for angiocardiology to define exactly the complicated and unusual vascular anomaly. This procedure showed not only absence of the right pulmonary artery but also a patent ductus arteriosus measuring nearly 1.5 cm. in diameter and bringing a large amount of contrast medium to the descending aorta. An interauricular defect was also evident. Roentgenkymography demonstrated the difference in pulsations on the two sides.

In cases of isolated absence of a pulmonary artery, where no clinical symptoms exist and the general condition of the patient is good, surgery is not indicated. In other cases, such as the one reported here, where a patent ductus arteriosus may cause pulmonary hypertension and a right ventricular load, one may consider tying off the ductus to avoid cardiac failure or a pneumonectomy to control hemoptysis.

Eleven roentgenograms; 8 diagrams; 1 electrocardiogram.

ILONA D. SCOTT, M.D.

Lewisburg, W. Va.

**Pulmonic Stenosis Due to Compression of the Pulmonary Artery by an Intrapericardial Tumor.** John A. Waldhausen, Carlos R. Lombardo, and Andrew G. Morrow. *J. Thoracic Surg.* 37: 679-686, May 1959. (National Heart Institute, Bethesda, Md.)

Although a significant percentage of mediastinal tumors arise within the pericardial space, only rarely does their presence cause impairment of cardiac function. When this does occur, it is usually attributable to impaired diastolic filling from generalized compression of the heart by the infiltrated pericardium or from cardiac tamponade due to fluid accumulation. Only rarely has obstruction to right ventricular outflow been described in association with an intrapericardial mass.

The authors report the case of a 23-year-old man in whom a primary mesothelioma of the pericardium compressed the pulmonary artery and produced the physical findings of obstruction to right ventricular outflow. A pressure gradient between the ventricle and pul-

monary artery of 47 mm. Hg was demonstrated at cardiac catheterization. The patient's initial history of an upper respiratory infection with fever, associated with radiographic and electrocardiographic evidence of pericarditis, suggested a localized abscess or collection of sterile fluid as the nature of the mass. The possibility of an aneurysm of the pulmonary artery or aorta was also considered. A selective right ventricular angiogram demonstrated the extrinsic character of the obstruction and its anatomic relations. Following excision of the tumor, the systolic murmur and thrill were no longer evident.

Five roentgenograms; 2 photographs; 1 photomicrograph; 1 electrocardiogram.

**Hereditary Hemorrhagic Telangiectasia and Pulmonary Arteriovenous Fistula. Survey of a Large Family.** Corrin H. Hodgson, Howard B. Burchell, C. Allen Good, and O. Theron Clagett. New England J. Med. 261: 625-636, Sept. 24, 1959. (Mayo Clinic, Rochester, Minn.)

Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease) is a congenital vascular disease manifested by the formation of localized arteriovenous capillary connections that are really tiny arteriovenous fistulas. The disease is transmitted by a simple dominant character and may skip individuals but probably not an entire generation. Groups of tiny ruby lesions are seen externally on the face, nasal and buccal membranes, lips, skin, and nailbeds. They may occur also in the internal organs, producing hemoptysis, gastrointestinal bleeding, hematuria, and cerebral hemorrhage. Two hundred and thirty-one members of a family with this disease were studied and 39.4 per cent were found to be affected. Among these were some who suffered from important complications, such as bleeding and disturbances of the central nervous system.

Fourteen of the 231 members of the family were found to have pulmonary arteriovenous fistulas. This is an incidence of 6.1 per cent of the group studied, or 15.4 per cent of those having telangiectasis. In 6 of the 14 the fistula was productive of symptoms.

Pulmonary arteriovenous fistula is a serious part of a generalized vascular dysplasia. It may cause distressing symptoms, may require surgical removal, or may endanger the life of the patient.

All members of families known to have hereditary telangiectasis should have periodic x-ray studies of the thorax in a search for fistula whether or not they have symptoms. By means of conventional roentgenograms, roentgenoscopy, tomograms, or angiocardiograms, a diagnosis can be made in nearly all cases.

The shadow of the fistula is usually seen in the frontal projection, though occasionally it may be hidden behind the shadow of the heart or diaphragm. In a few cases in which multiple tiny fistulas are present, no abnormality is evident on the roentgenogram. The shadows produced by the fistulas vary in size and shape. They may be round or lobulated, and they may be multiple. Usually they are of homogeneous density and are fairly well circumscribed. Examination in two projections shows that the lesion is within the parenchyma of the lung, but often close to a pleural surface. In most cases large vessels can be seen connecting the lesion to the hilus. Evidence of calcification is seldom present, though it has been reported.

Fluoroscopic observation discloses pulsation of the fistula and its vascular connections in more than half

the cases. In addition, the size of the shadow may change with changes in intrathoracic pressure. For example, with the Müller maneuver (deep inspiration against the closed glottis) the size of the fistula may be seen to increase. On the other hand, with the Valsalva maneuver (expiration against the closed glottis) the shadow of the fistula may become smaller.

Tomography helps demonstrate the vessels that lead to and from the hilus; it also helps identify multiple lesions, and it may demonstrate the cirroid character of the lesion. Venous angiocardiology will be diagnostic in all but a few cases, such as those with minute telangiectases. Serial films will show the medium entering the afferent vessel, filling the fistula, and returning to the heart by means of the efferent vessel.

Eight roentgenograms; 5 photographs; 2 charts; 2 tables.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Abnormal Congenital Fistulous Communications of the Coronary Arteries.** Guido Currarino, Frederic N. Silverman, and Benjamin H. Landing. Am. J. Roentgenol. 82: 392-402, September 1959. (Children's Hospital, Cincinnati 29, Ohio)

This paper reports 3 instances of congenital fistulous communications between a coronary artery and a cardiac chamber and reviews this group of developmental anomalies. In 1 of the authors' cases, a fistulous communication between an enlarged right coronary artery and the right ventricle was demonstrated by retrograde aortography. The second case was that of an infant who, at autopsy, showed an enlarged supernumerary aortic coronary artery emptying freely into the right atrium. In the third case autopsy revealed a congenital atresia of the pulmonary artery orifice with intact ventricular septum and an enlarged right coronary artery which communicated freely with the lumen of the right ventricle.

Abnormal communications involving the coronary arteries consist of a gross fistulous connection between the main coronary artery, or one of its branches, and (1) structures outside the heart, (2) the main pulmonary artery, (3) another coronary artery, (4) a coronary vein or the coronary sinus, or (5) a cardiac chamber. The coronary artery involved may be one of the two normal vessels or a supernumerary artery originating from the aorta or the pulmonary artery. The nature of these malformations is not certain but, since microscopic anastomotic channels normally connect the coronary arteries with all the structures mentioned above, it is possible that they are the result of dilatation of normal channels rather than anomalies which have developed *ex novo*.

The literature is reviewed and some aspects of the various types of communications are discussed.

The clinical findings in congenital coronary fistulas are described. Roentgenographically, the cardiac silhouette is normal in many cases. Cardiomegaly, enlargement of the main pulmonary artery, prominence of the intrapulmonary vasculature, and "hilar dance" have been noted in some instances. The presence of a large coronary artery aneurysm may be suspected from the roentgenographic study or at fluoroscopy. Cardiac catheterization is of limited value, as in general it is not possible by this method to distinguish the shunt produced by a coronary fistula from other types of shunt. The anomaly can be demonstrated by angiocardiology and by retrograde aortography.



The prognosis is generally fairly good, in contradistinction to the prognosis in a case of a fistula produced by the rupture of an aortic sinus of Valsalva. Many of the patients are asymptomatic. Death could be attributed to the lesion only in a few subjects. Disappearance or improvement of the signs and symptoms following surgical correction has been reported. The operation consists of ligation and sometimes also of division of the fistula, after it has been ascertained that no untoward effect results from temporary digital occlusion of the abnormal channel.

Seven roentgenograms; 1 photograph; 2 diagrams; 1 table.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

**Successful Repair of Sinus of Valsalva-Left Atrial Fistula.** Jerome Harold Kay, Robert M. Anderson, Reuben R. Lewis, and Martin Reinberg. *Circulation* 20: 427-429, September 1959. (University of Southern California School of Medicine, Los Angeles, Calif.)

What is believed to be the first case of a fistula resulting from rupture of a sinus of Valsalva into the left atrium is reported. The fistula was closed surgically by open heart surgery, with use of a heart-lung apparatus.

The patient was a woman of thirty-nine complaining of weakness, episodes of faintness, and exertional dyspnea. Plain films showed a 6-cm. mass continuous with the posterolateral aspect of the heart. Heart catheterization and angiocardiology failed to determine if the mass was intra- or extracardiac. Exploratory thoracotomy was done in anticipation of finding an extracardiac tumor but the mass was found to be in the left atrium. The incision was closed until the heart-lung apparatus could be used. At the second operation, about seven weeks after the first, the mass was found to be an intramural false aneurysm communicating with a sinus of Valsalva by a 7-mm. opening and with the left atrium by several minute openings. Successful closure was done, with relief of symptoms and return of the cardiac shadow to normal.

Two roentgenograms; 1 diagram.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**The Effect of Arteriovenous Fistulae on the Vascular Pattern of the Femora of Immature Dogs. A Microangiographic Study.** Patrick J. Kelly, Joseph M. Janes, and Lowell F. A. Peterson. *J. Bone & Joint Surg.* 41-A: 1101-1108, September 1959. (Mayo Clinic, Rochester, Minn.)

The fact that an arteriovenous fistula would increase bone length was first noted in 1870 by Broca. Subsequent investigations have related this increased growth to the increased blood supply resulting from the fistula formation.

In the present study an arteriovenous fistula was established in one hind limb of each of 16 immature dogs (before epiphyseal closure) with the opposite hind limb serving as the control. The dogs were observed for nine to fifteen months before being killed. Twelve had successful, well functioning fistulas. One month following surgical formation of the fistula and one month before the animal was killed, temperatures were recorded from the surface of the femur at the greater trochanter, at the middle of the shaft, and near the femoral condyle by means of thermistors mounted in needles. Specimens were prepared for microangio-

graphic study by means of injection of a suspension of barium sulphate in gelatin. Gross arteriograms of the abdomen and both hindquarters were obtained before removing the femurs and tibias. The fistulas were then carefully dissected and their diameters measured. The bones were sectioned and approximately 1,000 microangiograms were obtained in the 16 animals.

Three definite changes occur in the limb of a dog with a well functioning fistula in the hind limb:

1. Elevation of the temperature on the surface and in the intramedullary portion of bone
2. Lengthening of the femur
3. A definite alteration in the blood supply of the femur as indicated by microangiograms.

The microangiographic findings include:

1. Hypervascularity (more filled vessels than on the control side) of the small vessels, including capillaries of the medullary portion of the femur
2. Increase in the cortical and periosteal blood supply, particularly in the posterior distal half of the femur and in the region of the distal femoral epiphysis
3. In some animals a degree of dilatation of the individual vessels.

Two arteriograms; 9 microangiograms; 4 photographs; 1 drawing.

JOHN F. RIESSER, M.D.  
Springfield, Ohio

**The Identification and Quantification of Left-to-Right Circulatory Shunts. A New Diagnostic Method Utilizing the Inhalation of a Radioactive Gas, Kr<sup>85</sup>.** Richard J. Sanders and Andrew G. Morrow. *Am. J. Med.* 26: 508-516, April 1959. (National Heart Institute, Bethesda, Md.)

A method for the detection, localization, and quantification of left-to-right circulatory shunts by the inhalation of an inert radioactive gas, Kr<sup>85</sup>, is described. In the course of cardiac catheterization patients inhale the gas for thirty seconds, during which integrated blood samples are drawn simultaneously from a systemic artery and a right heart chamber or the pulmonary artery. A total of 125 Kr<sup>85</sup> tests were performed in 80 patients. This number included 69 tests in patients with proved shunts and 56 "control" tests in 45 patients with rheumatic heart disease or congenital heart disease without left-to-right shunts.

In the "control" tests, the radioactivity of the pulmonary arterial or right heart sample was always less than 15 per cent of that in the systemic arterial sample. Among the 69 tests performed in patients with proved shunts, the ratio exceeded 20 per cent in all but 6 instances, when it was between 15 and 20 per cent. The magnitude of the shunt could also be estimated by comparing pulmonary and systemic arteriovenous differences in Kr<sup>85</sup> content.

In all patients N<sub>2</sub>O tests were performed in the same chambers in which Kr<sup>85</sup> tests were carried out; in patients with shunts, determinations of blood oxygen content were also made. In every instance the results of the Kr<sup>85</sup> and N<sub>2</sub>O tests were comparable and both methods were superior in diagnostic accuracy to oximetry. With the Kr<sup>85</sup> test, shunts resulting in pulmonary-to-systemic flow ratios of 1.1:1 could be uniformly detected. The Kr<sup>85</sup> content of blood samples was determined with a Geiger counter and the results of the test were available within a few minutes. The Kr<sup>85</sup> test thus combines the accuracy of the N<sub>2</sub>O test with a simple and rapid technic of analysis.

Seven figures.

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## THE DIGESTIVE SYSTEM

**Gastrointestinal Radiology.** F. E. Templeton. *Am. J. Digest. Dis.* 4: 661-681, September 1959. (455 Medical-Dental Bldg., Seattle 1, Wash.)

This paper is a review of the progress in radiology of the digestive system in the past twenty-five years. In respect to equipment and technic, the author considers the most significant advance to have been the use of the spot machine as an adjunct to fluoroscopy. He mentions also photoelectric timers and their importance for satisfactory spot-filming.

Rapid serial filming and motion pictures are related developments which have come to the fore in the past ten years. Rapid film-changing devices have made possible a study of the motions of the esophagus and the act of swallowing. Image intensification, introduced in 1948, has added greatly to the value of motion pictures as a teaching method. Recently the intensified image has been projected through closed television, and the televised image has been recorded on tape as well as on film.

Higher kilovoltages (up to 150 kv) have become available in diagnostic equipment, but the author is not convinced that these will displace good spot fluoroscopy and double-contrast procedures.

Contrast media have shown less improvement than recording methods. Barium is still the standby, but the introduction of suspensory agents and mucosal irritants have improved examination of the small intestine and colon. Numerous oral contrast media have been introduced for demonstration of the gallbladder, their chief advantage being the modification of unpleasant side-effects. The use of an intravenous preparation for visualization of the bile ducts is a more significant advance.

No agent has been developed for successful visualization of the pancreas. Thorotrast, used twenty-five years ago to show the liver and the spleen, is no longer accepted, because of its radioactivity. Splenoportography with water-soluble media is valuable for studying the causes of portal hypertension and for demonstrating esophageal varices.

Water-soluble preparations are also injected directly into the gallbladder and biliary ducts at peritoneoscopy and during surgery for exploration of the ducts. Injections of the common ducts made through the "A-tube" after the patient leaves the operating room permit the ducts and the retained stones to be shown clearly.

Certain drugs have come into use as adjuncts to radiographic diagnosis. Proanthine has been found to decrease the irritability of the duodenal bulb, but it also causes gastric retention. Morphine contracts the sphincter of Oddi and holds the contrast medium in the common ducts. Urecholine speeds the passage of barium through the small intestine.

Having considered the technical aspects indicated above, the author turns to some of the newer knowledge that has gradually accumulated over the past quarter of a century. This he summarizes under the headings: Studies in Deglutition, Studies in Esophageal Motility and Structure, Cardiospasm, Lesions of the Esophagus, Lesions of the Stomach and Intestines. For his observations in these fields the reader is referred to the original paper.

The great advance in the examination of the small intestine from the technical standpoint is the introduc-

tion of barium through an intubation tube. Patterns formed by the small intestinal mucosa are studied extensively by this technic. A variety of conditions cause similar patterns, such as vitamin deficiencies, sprue, Whipple's disease, malabsorption syndrome, and even certain psychological states. The folds are coarse, rough, and sometimes jagged compared to the even, lace-like pattern of the normal mucosa. Often the barium pools or becomes segmented.

Dr. Templeton believes that in the future roentgenological methods will play an even more important role in the study of the gastrointestinal tract, for the science of radiology is a technical process used to study physiology, pathology and anatomy.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

**A Preliminary Statistical Survey of Carcinoma of the Oesophagus in the African with Special Reference to Acquired Oesophageal Fistulae.** Joseph Katz and George Cohen. *South African M. J.* 33: 773-775, Sept. 12, 1959. (Non-European Hospital, Johannesburg, Union of South Africa)

The authors had seen 120 cases of esophageal carcinoma at the Johannesburg Non-European Hospital from 1955 to the time of this report. Of these cases, 10 were in females, a proportional incidence considerably less than that in other surveys. The difference, it is said "may well be the result of a greater consumption of carcinogen-containing alcoholic beverages by the African male."

Adequate esophagoscopic records of the esophageal site were available in only 50 cases. The mass presented in the upper third in 13 (26 per cent) of these, in the middle third in 32 (64 per cent); in the lower third in 5 (10 per cent). Radiologically the statistics in a series of 29 unselected consecutive cases examined in 1957 showed 11.5 per cent in the upper third; 77 per cent in the middle third; 11.5 per cent in the lower third. The difference in percentage of levels between the two procedures may be due to the fact that the lesion appears 2 to 3 cm. higher on esophagoscopy. The preponderance of carcinoma at the level of the middle third in the present series (as opposed to the lower third in such series as that of Shanks and Kerley: *A Text-Book of X-Ray Diagnosis*. Philadelphia, W. B. Saunders Co. 1950, 2d ed.) suggests the possibility of a different etiological factor, which may well be, as mentioned earlier, a carcinogen-containing drink.

Of the 29 cases studied roentgenologically in 1957, fistulas were present in 13, the direction being into the mediastinum in 6 (46 per cent); into the respiratory tree in 5 (38 per cent); into a pleural cavity in 2 (15 per cent). All but 3 of these fistulas were attributable to the growth. Only 1 patient presented with the severe fulminating symptoms that other authors have noted in similar cases. The expected evidence of gangrenous pneumonitis and mediastinitis was absent.

Three case reports are given with accompanying roentgenograms: one each of an esophagopleural, an esophagobronchial, and an esophagomediastinal fistula.

**Carcinosarcoma of the Oesophagus.** C. J. B. Muller. *South African M. J.* 33: 775-777, Sept. 12, 1959. (University of Stellenbosch, Stellenbosch, Union of South Africa)

In the course of 12,000 barium-meal examinations in white and nonwhite patients, the author has encountered

only 1 case of sarcoma of any type in the esophagus. The patient was a 45-year-old Negro male who was referred for difficulty in swallowing and a sensation of obstruction in the middle of the chest of *one month duration*. The roentgen appearance was of special interest as an intramural, extramucosal origin of the tumor was suggested by four features: a cupola effect with sharply defined margins above and below; distention of the esophagus, with absence of the mucosal pattern; a smear effect resulting in a web-like pattern as barium passed over the tumor; constancy of shape on respiration, unlike a cystic tumor. The short duration of the symptoms indicated a malignant process, but the absence of ulceration and irregularity of contour were quite unlike carcinoma.

The patient died on the twelfth postoperative day. The pathological report described "a large greyish tumour 10 cm. in diameter, which appeared to be a carcinosarcoma consisting of a squamous-cell carcinoma and a spindle-cell sarcoma filling the esophagus."

It is impossible to make a diagnosis of carcinosarcoma solely on the basis of the roentgen findings. Myomas and other sarcomas, as melanosarcoma and leiomyosarcoma, may also present as extramucosal lesions, exhibiting sharply defined rounded defects, some with ulceration. With a short clinical history, the diagnosis of sarcoma is a reasonable certainty.

Two roentgenograms.

**Cineroentgenographic Studies of Gastrointestinal Motility in Healthy Subjects and in Patients with Gastric or Duodenal Ulcer, with Special Reference to Various Methods of Gastrectomy and the Dumping Syndrome.** S.-O. Liljedahl, O. Mattsson, B. Pernow, and S. Wallensten. *Acta chir. scandinav.* 117: 206-214, 1959. (Karolinska Institutet, Stockholm, Sweden)

Using the cineroentgenographic technic with the image amplifier, the authors studied the motility pattern of the stomach, duodenum, and small intestine in patients who had undergone various types of gastrectomy, and compared the results with those in healthy persons without gastrointestinal complaints. Attention was focused particularly on patients with the so-called dumping syndrome after partial gastrectomy by the Billroth II method. The material consisted of 22 patients with gastric or duodenal ulcer—3 nonoperated, 5 after partial gastrectomy by the Billroth I method, 14 (7 asymptomatic, 7 with the dumping syndrome) after Billroth II gastrectomy; 2 patients who had undergone total gastrectomy for carcinoma of the stomach; 6 normal persons.

After partial gastrectomy by the Billroth I method, the motility pattern in the stomach remnant was found, in all essentials, to resemble that in healthy persons. Thus, motility was sparse in the body of the stomach, whereas, deep waves of contraction were observed in the caudal part (corresponding to the gastric canal). In the gastroduodenostomy region, a pyloric mechanism had developed, in which the part of the duodenum included in the anastomosis acted as a sphincter. Antiperistaltic movements in addition to normal peristalsis were visible in the duodenum. A similar motility pattern was observed in patients in whom Billroth I gastrectomy had been complemented by vagotomy.

In most of the patients who had undergone partial gastrectomy by the Billroth II method, the barium suspension was seen to pass through the stomach with great rapidity. Only in patients with antecolic gas-

troenterostomy was there some retention of the medium in the stomach remnant. No definite difference could be detected between patients with and without the dumping syndrome as far as passage through the stomach was concerned. When the contrast medium reached the small intestine, however, peristalsis was considerably livelier in the patients with dumping than in those who were asymptomatic.

Four patients with the dumping syndrome were re-operated upon; in 3, the Billroth I method was used and in the fourth von Haberer's modification of this procedure. Examination one to two months later showed emptying to take place with considerably less precipitation than before re-operation. The contrast medium passed through the small intestine at an ordinary rate, except in 1 case, in which passage was apparently more rapid than normal.

Fifty-six cineroentgenograms; 1 table.

**The Prepyloric Septum: A Rare Anomaly.** J. Thompson Rowling. *Brit. J. Surg.* 47: 162-166, September 1959. (The Royal Hospital, Sheffield, England)

The prepyloric septum is a rare congenital anomaly presenting characteristic anatomical, clinical, and radiographic appearances permitting exact diagnosis. A thin diaphragm, consisting wholly of mucosa and containing neither muscle nor fibrous tissue, is found approximately 2 cm. proximal to the pylorus. A small orifice, 2 to 3 mm. in diameter, is present in the diaphragm, usually situated to one side of its center, the edge being soft and free from fibrosis, but of sufficient strength to resist dilatation. A review of the literature shows 2 previously recorded cases in infants and 5 in adults; these are briefly summarized. It is suggested that the condition represents a partial persistence of the epithelial occlusion stage characteristic of early gut development during embryonic growth.

The most common clinical feature as exhibited by adults is vomiting, frequently rather effortless, with little or no pain and no bleeding.

The radiographic appearance is pathognomonic. The septum is outlined as a thin, knife-like, constant filling defect of a truly linear nature occurring in the pre-pyloric region and unassociated with disturbances of peristalsis. The small segment of antrum distal to the septum can be readily filled despite the usually minute opening through the septum.

Treatment is surgical; simple excision of the septum will suffice. Most cases reported previously have been managed by partial gastrectomy or other major procedures but the author feels that these are unnecessary provided the nature of the lesion is recognized.

Two cases are reported. The first patient was a white male of unstated age with a twelve-year history of intermittent vomiting, abdominal discomfort, and ulcer-like symptoms. The lesion was not recognized at radiologic study, presumably because of the closer than usual association with the pylorus. Excision of the septum resulted in complete cure.

The second patient, a 68-year-old white male, gave an eighteen-year history of sporadic episodes of vomiting and epigastric pain, prone to follow eating of coarse foods. In this instance the lesion was recognized radiologically, although it was thought to be associated with gastric ulcer and scarring, which were not found at subsequent surgery. Partial gastrectomy was followed by uneventful recovery.

One roentgenogram; 1 photomicrograph; 2 diagrams.  
JAMES W. BARBER, M.D.  
Cheyenne, Wyo.

**Pernicious Anemia and Gastric Carcinoma.** M. Siirala, E. Erämaa, and J. Tapiovaara. *Acta med. scandinav.* 164: 431-436, 1959. (Maria Hospital, Helsinki, Finland)

In an investigation of the incidence of gastric carcinoma in pernicious-anemia patients and their relatives, 69 patients with pernicious anemia treated during 1957 in the hematological outpatient department of the Maria Hospital, Helsinki, were studied by the following procedures: x-ray examination of the stomach, gastros-copy, gastric biopsy, histamine test, uropepsin excretion, and Schilling test. Three control series were also examined.

All 69 patients had macrocytic, hyperchromic, and megaloblastic anemia at the time the diagnosis of pernicious anemia was made, and all responded adequately to treatment with vitamin B<sub>12</sub>. All had histamine achlorhydria.

The incidence of gastric carcinoma in the total pernicious-anemia series was 7.5 per cent; in those patients over sixty years of age it was 9.8 per cent. This incidence was significantly higher than the frequency of gastric carcinoma detected in the total population in Finland during 1954. It was also significantly higher than the incidence of gastric carcinoma (3.0 per cent) in 495 patients over fifty-five years of age admitted for x-ray examination of the stomach during 1957 in the same outpatient department. Benign polyps were found in 6.0 per cent of the patients in the pernicious-anemia series and in 1.2 per cent of the controls.

Twelve of 963 relatives of 60 pernicious-anemia patients had gastric carcinoma, as compared to 4 of 911 relatives of 54 patients without pernicious anemia. This difference is statistically significant.

One table.

**Gastric Pseudodiverticulum Secondary to Pancreatic Pseudocyst.** Peter J. Kapo. *Pennsylvania M. J.* 62: 1339-1340, September 1959. (Pennsylvania Hospital, Philadelphia 4, Penna.)

A case of gastric pseudodiverticulum secondary to pancreatic pseudocyst, in a 49-year-old male, is reported. In the two weeks preceding his admission to the hospital, the patient had had a cough and left chest pain accompanied by an abundance of yellow sputum. In the last six days of that period epigastric discomfort and vomiting of bitter green matter were superimposed. Pain radiated into the right and left upper quadrants. There had been similar episodes in the past two years. From the physical examination, diagnostic possibilities considered were lobar pneumonia, recurrent pancreatitis, hepatitis, pyelonephritis, and viscus perforation.

A postero-anterior chest roentgenogram showed a dense narrow horizontal strand of parenchymal infiltration at the left base fused with a shadow of a slightly elevated left hemidiaphragm. The superjacent lung was "congestively hazy." Several centimeters below, at the splenic level, a spherical gas pocket 3 cm. in diameter appeared to contain a shallow fluid level. A barium meal examination in the upright position revealed a shift of the stomach medialward. In the supine position, a surprising crescent-shaped tubular sac of barium, approximately 1 by 9 cm. and originating on the cardiac greater curvature, arched over the gastric

fundus. Upon rotation into the right posterior oblique position the medium flowed out and a double-contrast air-filled crescent appeared. The roentgen diagnostic considerations were diverticulum or accessory pocket incident to gastric perforation, and an extragastric inflammatory mass.

At laparotomy, a massive retrogastric quadrilobular pancreatic pseudocyst nestling within the lesser omental sac was discovered. One of the loculations impinged upward into the gastric fundus. One thousand cubic centimeters of pancreatic juice was aspirated and the cyst was marsupialized. On barium-meal examination, about one month postoperatively, the contour of the gastric fundus appeared normal. The gastric pseudodiverticulum was apparently created by a forceful invagination of the pancreatic pseudocyst into the gastric fundus.

Four roentgenograms.

**Diagnosis and Treatment of Acute Intestinal Intussusception with Controlled Insufflation of Air.** Eduardo S. Fiorito and Luis A. Recalde Cuestas. *Pediatrics* 24: 241-244, August 1959. (L. A. R. C., Alvear 863, Rosario, Sante Fe, Argentina)

In recent years the barium enema has been used in both the diagnosis and treatment of intussusception. The authors describe a new method which they term "controlled insufflation." It consists of insufflation of the colon with air under fluoroscopic and manometric control. When the intra-intestinal pressure arrives at the level selected for the particular case, a relay operates a tire-type valve, releasing gas, thus making impossible higher pressures than are desired.

A plain film of the abdomen in the upright position demonstrates the intussusception in many cases. A nonlubricated Foley bag catheter is introduced into the rectum and inflated with 40 to 50 ml. of air. The diagnostic stage is started by insufflating the colon slowly, working with a gas pressure of not more than 60 mm. Hg. Another roentgenogram is then obtained. In a few instances this pressure is enough to reduce the intussusception, but in most cases, if there are no medical contraindications, one may proceed to the therapeutic stage, working with a gas pressure of 130 mm. Hg. This pressure is maintained until the gas completely fills the small bowel. Two roentgenograms, frontal and lateral, are taken at this moment.

From August 1954 to December 1958, 86 cases of intussusception were treated by insufflation; full reduction was achieved in 94 per cent. Two of the 5 cases requiring surgery were of more than twenty-four hours duration. All patients were between three and eighteen months of age.

It is the experience of the authors and others that the results are much better with controlled insufflation than with the barium-enema procedure.

Five roentgenograms; 1 drawing.

**Volvulus Associated with Pregnancy: A Review and a Report of 3 Cases.** George D. Malkasian, Jr., John S. Welch, and George A. Hallenbeck. *Am. J. Obst. & Gynec.* 78: 112-124, July 1959. (The Mayo Foundation, Rochester, Minn.)

Only 43 cases of intestinal volvulus complicating pregnancy have been reported in the English language. Three additional cases from the Mayo Clinic are presented here. The overall maternal mortality rate in the cases from the literature was 27.9 per cent with an

identical fetal mortality rate. When the volvulus involved the small bowel the mortality rate rose to 35.7 per cent for both mother and fetus.

Volvulus in primigravidae women was almost twice as frequent as in multiparous patients. Two of the previously reported cases occurred in the first trimester of pregnancy, 9 in the second trimester, 25 in the third trimester (8 at term), and 5 in the postpartum period. Two were associated with ectopic pregnancies. The volvulus was located in the small bowel in 15 cases, the sigmoid colon in 14 cases, and elsewhere in the colon in the remainder. Both large and small bowel were involved in 5 instances.

The diagnosis of volvulus during pregnancy is difficult. Vomiting is often attributed to the pregnancy, and the cramping lower abdominal pains to threatened abortion, Braxton Hicks contractions, or premature or early labor. The resultant delay in seeking medical advice or in definitive treatment has accounted for the high mortality.

An abdominal film may be of considerable help, as is amply demonstrated in the authors' third case. In general, the finding of an enormously dilated, isolated loop of intestine is all that is required for a suspicion of volvulus. In volvulus of the sigmoid the x-ray findings are characteristic and are not seen in any other condition. Although there may be alterations of expected location due to the uterine mass, two hugely dilated segments of sigmoid lie upright and parallel in the abdomen, usually on the left side. A visible column of air communicates between these two segments at their apex. In addition, lateral decubitus views may show fluid levels within the intestinal lumen.

The authors' 3 cases are of special interest. One is the fourth to be reported in English in which volvulus involved both the cecum and the terminal portion of the ileum and the second such case with maternal survival. Another is the only recorded instance of successful treatment by colonic intubation without surgical intervention.

Active surgical treatment for volvulus during pregnancy is recommended, particularly in cases in which signs of intestinal strangulation are present or in which relief is not afforded by conservative medical measures over a short period. Decompression of a sigmoid volvulus with a long rectal tube may be justified under certain circumstances, but subsequent definitive surgical treatment is usually necessary.

A comprehensive list of references is included.

Five roentgenograms; 3 tables.

ROBERT L. EGAN, M.D.  
University of Texas, Houston

**Coexisting Carcinoma and Diverticula of the Colon. A Review of Three Hundred Fifty-Five Cases of Carcinoma of the Colon.** Joseph L. Ponka, J. DeWitt Fox, and Brock E. Brush. *Arch. Surg.* 79: 373-382, September 1959. (The Henry Ford Hospital, Detroit, Mich.)

Diverticula and diverticulitis of the colon may give symptoms resembling carcinoma. Because of this there is some danger of actually overlooking a carcinoma when diverticula are seen on the roentgenogram.

Three hundred and fifty-five cases of adenocarcinoma of the colon were seen between 1953 and 1957 in the Department of General Surgery of the Henry Ford Hospital, Detroit, Mich. In 75 cases (21 per cent) there was associated diverticulosis. The incidence of disease was greatest in the sigmoid, where there were

197 cases of cancer with 56 cases of associated diverticulosis and diverticulitis (28 per cent).

There were cases where it was difficult to differentiate between diverticulitis and carcinoma. The attitude recommended in this situation is one of surgical aggression, in that there is much less danger in removing a portion of the colon for diverticulitis with the impression that it is carcinoma, than it is to leave a carcinoma untreated because it is thought to be diverticulitis.

There were 35 cases in the sigmoid in which the carcinoma and diverticula were so closely related that there was great difficulty in accurate radiologic diagnosis. The overall accuracy of the roentgen diagnosis of carcinoma in 335 cases was 94 per cent, but in only 16 (48 per cent) of the 35 cases cited could carcinoma be differentiated roentgenologically from diverticulosis or diverticulitis. This points to the need for surgical resection in equivocal cases such as those with complete obstruction, poor filling, atypical lesions with long, poorly filled segments, and those with short, poorly filled segments with diverticula.

Two case reports are included.

Four roentgenograms; 2 diagrams; 4 tables.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Roentgenologic Findings in Ulcerative Colitis with Malignant Degeneration.** N. P. G. Edling, R. Lagercrantz, and H. Rosenqvist. *Acta radiol.* 52: 123-128, August 1959. (Karolinska Sjukhuset, Stockholm, Sweden)

The authors investigated 26 cases of ulcerative colitis with malignant degeneration. Two-thirds of these had advanced inflammatory changes in a chronic stage, and one-third showed roentgen evidence of improvement of the colitis. Only 15 per cent of the growths were situated at the rectosigmoid junction, 85 per cent appearing elsewhere in the colon.

The investigation indicates that there is no consistent characteristic in the roentgen picture of the colon with ulcerative inflammatory changes and subsequent development of carcinoma. The material also shows that severe changes in the wall due to colitis may heal without fibrosis of the muscular layer and the serosa. This healing, if it occurs, is however no guarantee against malignant change even though the symptoms may have decreased or even disappeared.

Six roentgenograms.

THEODORE E. KEATS, M.D.  
University of Missouri

**Toxic Megacolon in Ulcerative Colitis.** James L. A. Roth, A. Valdes-Dapena, G. N. Stein, and H. L. Bockus. *Gastroenterology* 37: 239-255, September 1959. (Graduate Hospital, Philadelphia 46, Penna.)

Toxic megacolon is the most dreaded complication of a fulminating attack of ulcerative colitis. It consists in extreme dilatation of part or all of the diseased colon and may occur during a fulminating first attack of colitis, during an acute relapse of the relapsing-remitting type of the disease, or in association with an exacerbation in a chronic course. In a review of the records of the Graduate Hospital, University of Pennsylvania, for the years 1943-1958, the authors found 15 examples, in 12 patients. Their observations are based on this series. The mortality for the group was 25 per cent.

The clinical picture is that of almost complete colonic obstruction with impending perforation. Profound



toxicity is a constant feature. Radiographs of the abdomen demonstrate gaseous distention primarily within the colon, particularly the transverse section. A barium enema may be required to rule out a mechanically obstructing lesion.

Therapy must be intensive and comprehensive, with complete bowel rest. It is felt that surgical measures should be avoided, if possible, during the acute phase. Six of the authors' patients were operated upon, with 2 deaths. There was 1 death among 6 patients receiving medical treatment only.

One illustrative case is reported.

Five roentgenograms; 5 photomicrographs; 4 tables.

MAJ. MARTIN A. THOMAS, M.C.  
MacDill AFB, Tampa, Fla.

**A Study of Pancreatography.** Martin Birnstingl. Brit. J. Surg. 47: 128-139, September 1959. (St. Bartholomew's Hospital, London, England)

An anatomical and histologic study was undertaken with a view to correlation of the radiologic appearance of the duct system of the pancreas and the histologic findings. The intention was to provide a basis for the interpretation of operative pancreatograms and to investigate the occurrence of epithelial changes in autopsy material. A total of 150 pancreatic and duodenal specimens were obtained in the course of routine autopsies on subjects presumably without pancreatic disease. In each specimen the main pancreatic duct was cannulated and injected with radiographic contrast material. The preparation was then radiographed, fixed, and subsequently sectioned.

The main emphasis in the paper is histologic and the observations are recorded in great detail. The author's own summary, with minor changes, follows:

1. As a result of combined radiographic and histological study in necropsy material, the common anatomical variations which influence the interpretation of pancreatograms have been reviewed. The main pancreatic duct showed variation in caliber ranging between maximum diameters of 1.8 and 9.2 mm.; it appears that the upper limit of the normal diameter of this duct is about that of an ordinary lead pencil (8 mm.). Appearances of isthmus stenosis, terminal dilatation, and an undulating outline were occasionally seen and represent anatomical variants. The accessory pancreatic duct communicated with the main ductal system in 68 per cent of specimens, but appeared patent in only 35 per cent.

2. Dilatation and irregularity of the secondary pancreatic ducts were commonly seen on the pancreatograms and produced an appearance of pancreatectasis in a few specimens. These variations closely reflected the development of hyperplastic and metaplastic changes in the ductal epithelium.

3. Columnar epithelial hyperplasia was seen in 29 per cent of organs; the change was most frequent in the secondary ducts and in the ampullary region of the accessory pancreatic duct. It was most common in the form of intraductal proliferation, but hyperplasia of mucous-secreting glandular structures related to the ducts was also seen. These variants resemble cholecystitis glandularis proliferans, with which they are comparable. Subclinical focal pancreatic necrosis was encountered in 5 specimens, in which it was apparently related to the presence of hyperplastic epithelial lesions in the ducts.

4. Squamous epithelial metaplasia was found in 10

per cent of organs, although never to the extent shown by columnar hyperplasia, with which the change was generally associated.

Five roentgenograms; 9 photomicrographs; 7 drawings; 2 tables.

JAMES W. BARBER, M.D.  
Cheyenne, Wyo.

**Spontaneous Disappearance of Gallstones.** W. van der Linden and Å. Hjelmstedt. Acta chir. scandinav. 117: 230-232, 1959. (Centrallasarettet, Östersund, Sweden)

The spontaneous disappearance of gallstones in a young woman during the postpartum period is reported. The patient suffered from typical biliary colic during the first few months of her second pregnancy but during the later months was symptom-free. After a full-term delivery, the biliary colic reappeared, with increasingly frequent attacks. Cholecystography about two months postpartum showed a normally visualized gallbladder, containing a large number of small stones. Operation was advised but was postponed for several weeks. During this time the patient suffered daily from violent upper abdominal pain, radiating to the right loin and associated with severe nausea and vomiting. There was no jaundice, but the urine was dark. At operation, no stones could be palpated nor could any be found when the gallbladder was opened. Cholangiography failed to disclose common duct stones. Histologic examination of the gallbladder specimen showed hypertrophy of the muscular layers, indicating that there had been an obstruction to emptying.

Two possible explanations for the disappearance of the gallstones are offered: (1) dissolution and (2) migration. The daily colic seems to favor the theory of migration.

Two roentgenograms.

**Renal Insufficiency After Oral Administration of a Double Dose of a Cholecystographic Medium. Report of Two Cases.** Robert M. Rene and Sherman M. Mellinkoff. New England J. Med. 261: 589-592, Sept. 17, 1959. (University of California School of Medicine, Los Angeles, Calif.)

The authors report 2 cases of renal insufficiency occurring after the oral administration of a double dose of iopanoic acid (Telepaque).

Serious reactions after oral administration of iopanoic acid are virtually unknown. This is in contrast to the parenteral injection of organic iodides, which has sometimes been followed by sudden death from anaphylactic shock, or delayed death in patients with pre-existing renal disease. The authors know of no previous report of renal insufficiency after oral cholecystography.

The relation between the azotemia which was observed in these two patients and the prior administration of iopanoic acid seemed more than fortuitous, yet the mechanism was not clear. There was nothing to suggest allergy or anaphylaxis, with the possible exception of transient orthostatic hypotension in one case, and the renal shutdown itself. An idiosyncrasy either to iodide or some other radical of iopanoic acid, particularly manifest when larger doses are used, is conceivable.

In animals iopanoic acid given orally is eliminated largely by way of the gastrointestinal tract and in dogs doses of as much as 1 gm. per kilogram of body weight have produced no evidence of impairment of renal function. In man, however, renal excretion



amounts to about 38 per cent of the administered dose, and dysuria is not an uncommon symptom. Renal irritation in susceptible persons may result in reflex vascular spasm, with partial or complete shutdown.

The authors conclude that it seems wise not to administer large doses of gallbladder medium to patients with evidence of pre-existing renal disease, or to do so, if necessary, only after the possible risk has been carefully weighed. One of their patients gave a past history suggestive of a low-grade pyelonephritis, and cultures of the urine during hospitalization yielded *E. coli*, *Klebsiella*, and *Aerobacter*.

Two tables. CHARLES M. GREENWALD, M.D.  
St. Cloud, Minn.

**Death After Cholecystography.** Basil Rifkind. Brit. J. Radiol. 32: 622-623, September 1959. (Royal Infirmary, Glasgow, Scotland)

It is frequently stated that hepatocellular or obstructive jaundice is a contraindication to cholecystography on the principle that the procedure may harm an already damaged liver. The author describes a case in which it is felt that the cholecystography was a contributing factor in the patient's death.

A 73-year-old housewife was admitted because of jaundice, which had appeared ten days earlier. The liver and spleen were not palpable, and there was no abdominal tenderness. The stools were pale and the urine contained bile but no urobilinogen. Liver function tests showed: alkaline phosphatase, 21 King-Armstrong units per cent; serum bilirubin, 30 mg. per cent; serum proteins, 6.5 gm. per cent (albumin, 3.5 gm.; globulin, 3.0 gm.); thymol turbidity, 2 units; thymol flocculation, 1 unit.

During the first few days after admission, the patient remained comfortable and was regaining her appetite. Inadvertently, a cholecystogram was carried out, with Phenobutidil (1-(2:4:6-triiodo-phenoxy)-butyric acid) in the recommended adult dose by mouth. Vomiting occurred the following day, coma ensued, and death followed on the fourth day. Postmortem examination revealed severe liver necrosis. The pathologist was of the opinion that the changes were of more than two weeks duration.

The author feels that it is not unreasonable to suggest that the medium acting on such a diseased organ may have been the final insult accounting for the patient's sudden deterioration. This experience tends to justify a cautionary attitude regarding cholecystography in the presence of jaundice.

JAMES F. MARTIN, M.D.  
Bowman Gray School of Medicine

## THE DIAPHRAGM

**Diaphragmatic Hernia in Infancy.** J. O. Reed and E. F. Lang. Am. J. Roentgenol. 82: 437-449, September 1959. (Children's Hospital of Michigan, Detroit 1, Mich.)

This report is based on a series of 48 cases of diaphragmatic hernia appearing in infants. Three groups of hernias were encountered. The largest group (31 cases) involved the posterolateral muscular segment of the diaphragm (pleuroperitoneal hernias). Hernias involving the esophageal hiatus were the next most common (12 cases) and those involving the anteromedial or tendinous segment of the diaphragm were the least common (5 cases).

Pleuroperitoneal hernias may be of serious consequence with a high mortality if not treated, due to cardiorespiratory failure in the newborn and strangulation of the bowel in older children.

Radiographic manifestations include: (1) incomplete visualization of the diaphragmatic leaf on the affected side; (2) visible loops of bowel in the thorax, appearing as multiple radiolucencies, perhaps containing fluid; (3) contralateral displacement of the heart; (4) reduction or absence of the abdominal intestinal gas pattern; (5) an esophagus of normal length. There may be compression atelectasis and hypoplasia or even aplasia of the ipsilateral lung. A hernia in this location may be of the sliding variety and be present at one time and not at another. If a hernia is suspected, it is advisable to delay feeding and reduce distention by aspiration to avoid cardiorespiratory embarrassment. The larger hernias associated with severe developmental defects of the lung result in early death. A certain number of these patients can be salvaged by immediate surgery providing the pulmonary defect is not too severe.

Certain radiographic criteria indicate the characteristics of the hernia. The size of the defect in the diaphragm as estimated by the size of the hernia may be deceiving, but this determination is largely of theoretical value since repair by an experienced surgeon is not limited to smaller defects. The presence of a hernial sac may be suspected if there appears to be limited herniation; whereas, free extension of abdominal contents into the thorax indicates the absence of a sac.

Esophageal hiatal hernias are of less clinical consequence and are usually found during investigations of feeding problems in older infants. Respiratory embarrassment is unusual. Contrast studies are necessary for satisfactory classification.

Hernias involving the anteromedial aspect of the diaphragm are encountered in older infants or children and are investigated because of complaints arising from the mechanical problems incident to the herniation.

Thirty-two roentgenograms.

JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Leiomyoma of the Diaphragm.** Jesse H. Meredith and H. H. Bradshaw. J. Thoracic Surg. 37: 641-645, May 1959. (Bowman Gray School of Medicine, Winston-Salem, N. C.)

Tumors of the diaphragm are rare, only 42 examples having been recorded in the literature. One-half of these tumors were malignant; only 1 was of smooth-muscle origin, a leiomyosarcoma. The authors report a case to emphasize the value of pneumoperitoneum in the diagnosis of diaphragmatic tumors and to call attention to the high incidence of malignancy in such tumors.

The patient, an asymptomatic 57-year-old woman, was admitted to the hospital because of a progressively enlarging shadow in the left lower chest demonstrated roentgenographically. There were dullness and absence of breath sounds in this area; the diaphragm descended on inspiration. Postero-anterior and lateral chest films showed the shadow above the diaphragm. A 1,500-c.c. pneumoperitoneum, induced in 500-c.c. stages, revealed the contour of the inferior surface of the diaphragm to be normal; above there was a mass which could not be differentiated from the diaphragm. The tumor was resected without difficulty. The pathologist's diagnosis was "leiomyoma of the diaphragm." The patient was observed for three years without recurrence. In an

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addendum to the paper, however, it is stated that six months following submission of this case report, chest roentgenograms disclosed a lesion of the right upper lobe. This was resected and proved to be a "spindle-cell malignant tumor." It is thought to be a metastases from the previous tumor.

In the study of this case, the authors found pneumoperitoneum to contribute far more information than fluoroscopy and pneumothorax. The value of pneumothorax may be limited by adhesions to the inferior surface of the lung. In resecting the tumor, preoperative pneumoperitoneum and/or crushing of the phrenic nerve will contribute to closure of the defect. The fact that half of the tumors of the diaphragm are malignant should be kept in mind when a mass in this area is encountered, and a wide margin of apparently normal tissue should be removed with the tumor.

Five roentgenograms; 1 photomicrograph; 1 photograph.

#### Transient Paradoxical Movement of the Diaphragm.

Raymond A. Gagliardi, Howard H. Feigelson, and Arthur S. Shufro. *J. Thoracic Surg.* 37: 636-640, May 1959. (Sinai Hospital, Detroit 35, Mich.)

Paradoxical motion of the diaphragm following phrenicotomy or associated with malignant involvement of the mediastinum is a familiar entity. It is less well known that this phenomenon can appear in nonmalignant pulmonary disease and in the absence of direct involvement of the phrenic nerve. The authors review the literature on paradoxical diaphragmatic movement and report a case in which paralysis of the diaphragm occurred concomitantly with pneumonia.

It is possible that unilateral paralysis of the diaphragm is more common than is generally suspected, since most cases of pneumonia are not studied fluoroscopically. The physical signs of diaphragmatic paralysis are easily missed or overshadowed by adjacent changes, especially in the presence of inflammatory pulmonary disease. The diagnosis of diaphragmatic paralysis is made by the demonstration of elevation of the diaphragm, as well as its paradoxical movement, at fluoroscopy. If the patient is asked to sniff sharply, the paradoxical motion is accentuated. In the authors' case, the paralysis cleared after a period of eight weeks.

The possibility of inflammatory involvement of the phrenic nerve as a cause of diaphragmatic paralysis is suggested.

Two roentgenograms.

### THE MUSCULOSKELETAL SYSTEM

**Hereditary Enchondral Dysostosis. Twelve Cases in Three Generations Mainly with Peripheral Location.** Per Ödman. *Acta radiol.* 52: 97-113, August 1959. (Länslasarettet, Håssleholm, Sweden)

The author discusses a condition which he terms hereditary enchondral dysostosis, with a presentation of 12 cases in three generations, mainly with peripheral location. This condition is known also as dysplasia epiphysealis multiplex and epiphyseal dysplasia.

Roentgenographically, the hereditary epiphyseal disturbances manifest themselves as changes in the ossification pattern of the epiphyses, and the conditions following such changes. The mode of inheritance varies.

The most marked roentgenographic changes, as well as the most prominent clinical signs, are observed in the knee joints, with the ankle joints next in impor-

tance as regards the extent and severity of the disturbances. The roentgenologic lesions are reflected in typical clinical manifestations. These first appear at about the age of three or four, in the form of walking difficulties, and gradually become aggravated up to the age of seven to fourteen, when the roentgenologic changes are most marked. Much discomfort, particularly in the knees and ankles, is experienced in connection with locomotion. These disabilities decrease during puberty, but are still present to some degree in the adult. The clinical signs are proportional to the roentgen appearances.

In 2 of the author's cases in children the femoral epiphyses are described as having an irregular porous structure; the bone contour was jagged, while the border adjoining metaphyses was smooth. Multipolar areas of ossification of the epiphyses may be seen. Irregularity of the bony structure of the epiphyses is observable during the entire period of growth.

Young persons with marked epiphyseal changes during growth are more or less disabled up to the time when the epiphyses have become completely ossified. When this stage is reached, clinical improvement is noted.

Contrary to earlier reports, the changes in the author's patients were situated only in the joints of the extremities. The clinical picture in adults was dominated by osteochondrosis.

Thirty-one roentgenograms; 1 genealogical tree.

THEODORE E. KEATS, M.D.  
University of Missouri

**Unusual Manifestations of Gout.** R. C. Rosenquist, C. S. Small, and P. H. Deeb. *Arch. Path.* 68: 1-10, July 1959. (P.H.D., Loma Linda Sanitarium and Hospital, Loma Linda, Calif.)

A severe case of tophaceous gout in a 70-year-old man is reported, with particular attention to the roentgen and pathologic findings. The patient first noticed joint pain when he was about fifty years of age. Five years later small nodules adjacent to the joints of the hands and feet were discovered. Progressive enlargement of the tophi occurred, and at the age of sixty-five, painful ulceration and chronic draining sinuses developed over the tophi. For this reason, the right fourth and fifth toes and the left fourth toe were amputated. Roentgen examination included multiple views of the hands, elbows, knees, and feet, and showed extensive calcium deposits, areas of bone destruction, and severe distortion of joint relationships.

The patient was started on probenecid, 0.5 gm. daily, with supplemental sodium bicarbonate to keep the urinary pH neutral or alkaline, but this program was not closely followed because of gastrointestinal irritation. The patient was subsequently hospitalized on five occasions, during which time his condition progressively deteriorated. Pain in the extremities and low back became almost continuous. Serum uric acid levels were consistently elevated, being in the range of 8 to 10 mg. per 100 ml. Fasting blood sugar was 123 mg. per 100 ml. The urine consistently showed protein, blood, and pus. At the time of final hospitalization, the nonprotein nitrogen was 114 mg. per 100 ml. At autopsy the remarkable feature of this case was the extremely wide distribution of urate deposits, including coating of all joint surfaces with urates. A large amount of calcific material was found in the larger joints, as well as the more common locations.

The bizarre appearance of gout makes it desirable to

consider this diagnosis in any case of painfully swollen joints. The roentgen picture is not pathognomonic; it may resemble that in such diseases as rheumatoid arthritis, degenerative arthritis, and Boeck's sarcoid.

Twenty-four figures, including 8 roentgenograms.

**Osteosclerotic Changes in Myelomatosis. Report of a Case.** Olle Odelberg-Johnson. *Acta radiol.* 52: 139-144, August 1959. (Malmö Allmänna Sjukhus, Malmö, Sweden)

The author presents a case of myelomatosis in which roentgen examination revealed progressive and widespread, circumscribed osteosclerosis resembling metastases but no evidence of osteolysis.

Histologic examination of a typical example showed many coarse bone trabeculae at the site of the lesions. Between the trabeculae were abundant plasma cells. There was cancellous bone outside the osteosclerotic areas containing fine bone trabeculae and the bone marrow was rich in cells.

A survey of literature suggests that this is a rare manifestation of myelomatosis.

Three roentgenograms.

THEODORE E. KEATS, M.D.  
University of Missouri

**Idiopathic Hypercalcemia. A Case Report with Assays of Vitamin D in the Serum.** David W. Smith, Robert M. Blizzard, and Harold E. Harrison. *Pediatrics* 24: 258-269, August 1959. (D. W. S., University of Wisconsin Medical School, Madison 6, Wisc.)

The authors report a case of prolonged hypercalcemia in which assays of vitamin D in the serum were performed. At ten months of age the patient presented a clinical picture of unexplained mild idiopathic hypercalcemia of infancy. No therapeutic measures were taken at this time to correct the hypercalcemia and at five years of age symptoms of severe idiopathic hypercalcemia were evident.

The osseous findings in this case are of considerable interest, since demineralization of bone was demonstrated. Roentgen studies showed subepiphyseal rarefaction, periosteal elevation, and relative rarefaction of the shafts of the long bones as compared to the epiphyses. These changes are similar to those described in cases of vitamin D intoxication in children by Ross (*J. Pediat.* 41: 815, 1952. *Abst. in Radiology* 61: 687, 1953) and others. Roentgenograms in the present case, however, did not disclose the markedly increased density at the epiphyseal plate which is usually found in both vitamin D intoxication and idiopathic hypercalcemia.

Various therapeutic measures were tried, including cortisone administration, a low calcium diet, and citrate therapy. The concentration of calcium in the serum returned to normal and remained so after two years. Also, the bone structure became normal.

The etiology of idiopathic hypercalcemia is discussed with particular reference to the role of vitamin D in the present case.

Six roentgenograms.

**Echinococcus Disease of the Calvarium.** E. Sami. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 91: 339-343, September 1959. (In German) (Pahlavi-Krankenhaus, Teheran, Iran)

Eighty-five per cent of hydatids are retained either in the liver or lungs, where the larvae have difficulty in

passing the capillary bed. Osseous involvement is rare, occurring in less than 3 per cent of the cases. Echinococcal lesions of the calvarium are most unusual, only 2 cases having been observed by the author against 22 intracerebral cases during the same period of time.

The first patient was a boy, aged 14, who for three years had noticed a gradually increasing occipital bulge. Repeated seizures without an aura had occurred recently, but headaches had been slight. Clinically, there was a fluctuating occipital soft-tissue bulge, the size of an orange, the base of which was surrounded by a sharp bony ridge. Examination revealed homonymous hemianopsia to the right. Roentgenograms showed a round 4-cm. defect in the midoccipital region. There was wide separation of the inner and outer tables, with periosteal proliferation of the outer border. Surgically, the condition proved to be echinococcal disease with numerous larger and smaller cysts covered by a thick membrane. The postoperative course was uneventful.

The second patient was a soldier, aged 23, who had suffered from morning headaches and dizziness for the past four months. Swellings, gradually increasing in number and size, had been noticed in the occipital region for the past three years. On examination, several soft-tissue bulges of the scalp were found posteriorly, surrounded by a sharp osseous ridge at the base. Neurologic findings were bilateral choked disk of slight degree, horizontal nystagmus, and a positive Romberg sign.

Roentgenograms revealed numerous osseous defects of the occiput and of the parietal bones posteriorly, with thin interwoven septa. The external table was partly intact but occasionally was eroded from the inside, with the production of a semilunar defect. The floor of the posterior fossa was thinned, and the sella turcica was slightly enlarged. The preoperative diagnosis was echinococcal disease.

At operation a thick covering membrane was again found. Beneath this were virtually hundreds of smaller and larger cysts which occupied the posterior third of the cranial cavity. After removal of all cysts a large defect remained, with the tentorium and the cerebellar hemispheres at the floor, and the occipital lobes above, covered by the dura mater. The latter had become so thin, as a result of compression, that the cerebral vessels underneath were clearly visible.

The patient made an uneventful recovery and was discharged two weeks postoperatively. After three more weeks the neurological findings were essentially normal.

Three roentgenograms. ERNEST KRAFT, M.D.  
Northport, N. Y.

**Radiologic Aspects of Moderately Severe Cervical Spine Trauma.** Martin S. Abel. *Arch. Phys. Med. & Rehabil.* 40: 371-378, September 1959. (655 Sutter St., San Francisco, Calif.)

Routine views of the cervical spine may be of little help in demonstration of the frequent injuries of the small elements of the cervical vertebrae. The author consequently has undertaken some anatomic studies to evaluate methods and projections which may more favorably demonstrate such minor trauma. Cadavers were subjected experimentally to oblique hyperextension and flexion maneuvers with forces comparable to those sustained in typical accidents likely to produce whiplash injuries. Special views of the uppermost and

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lowest segments of the cervical spine were found necessary to visualize the small fractures and fracture-dislocations produced. An occipital-submental view of the first cervical vertebra and upper cervical segments *en face* is obtained with the patient in prone position with the neck strongly hyperextended and the central beam, well-coned, directed through the skull from above downward at an angle 15° cephalad to the vertical plane through the head. A second special view is a modified anteroposterior projection, useful in demonstrating the posterior processes of the lower cervical vertebrae. For this the patient is placed supine, the head and neck are strongly hyperextended, and the beam, angled 30° toward the feet, is well coned to the lower cervical region. For both of these views the author prefers a fine-focal-spot, short-distance magnification technic (Radiology 66: 747, 1956).

These views, plus selected standard studies, were used to demonstrate small, easily overlooked compression fractures involving the facets on one side, short fractures through the joints of Luschka of one side, lateral compression and/or displacement of the superior facets at C-1 and C-2, and small degrees of abnormal rotation of the occiput at C-1. The illustrative roentgenographic reproductions are small, and points under discussion are not easily seen.

Small injuries of the cervical spine sometimes produce little immediate difficulty, but the patients return with severe symptomatic sequelae some years later. The special views under discussion may reveal such injuries at that time.

A review of over 1,000 routine frontal views of the chest was made as part of this study in an attempt to obtain a control series of normal individuals without cervical spine symptoms. In a high percentage minor deformities were found, increasing in frequency with age. It is said, for example, that 20 per cent of persons between forty-one and sixty will exhibit some of the deformities under discussion.

In anatomic studies of 31 cadavers, the necks were radiographed and then examined microscopically and grossly. Hypertrophic changes of the bodies of the vertebrae were found to occur independently of hypertrophic change of the apophyseal joints and *vice versa*. Hypertrophic arthritic changes in the apophyses were always associated with marked deformity or malalignment of these posterior joints, and the arthritis was centered maximally about the site of deformity.

The author concludes that hypertrophic changes of the vertebral bodies (as opposed to such changes in the posterior joints) are "largely a response to static weight-bearing stresses, whereas, apophyseal joint arthritis is a response to dynamic stresses consequent to alteration in the planes of motion. There is obviously an interrelationship in these two categories." It is felt that the disks, vertebral bodies, lateral joints of Luschka, and apophyseal joints are all components of the same suspension system so that changes or alterations in one part of the system must eventually be reflected in changes in other components.

It is evident that painstaking radiographic examination of the cervical spine is essential for demonstrating small lesions of the structures under discussion. Special views as described are frequently most helpful and may be necessary for proper diagnosis.

Seventeen figures, including 10 roentgenograms; 1 table.

JAMES W. BARBER, M.D.  
Cheyenne, Wyo.

### Significance of Survey Films (Plain Views) of the Lumbar Spine in Lumbar Intervertebral Disk Prolapse.

H. G. Stössel, C. W. Fassbender, and G. Häussler. Fortschr. a. d. Geb. d. Röntgenstrahlen 91: 329-334, September 1959. (In German) (C. W. F., Allgem. Krankenhaus Heidelberg, Tangstedter Landstr. 400, Hamburg-Langenhorn, Germany)

In 438 cases of sciatica and disk prolapse the most important diagnostic sign on the plain film was narrowing of the intervertebral space, a finding which corresponded to the surgical picture in 46 per cent of the cases. This was observed in 217 cases (50 per cent)—45 times with two disks involved; 10 times with involvement of more than two disks. The plain films were normal in 77 cases, although prolapse was demonstrated by myelography and at surgery.

Localized spondylosis deformans and dorsal disalignment gave indication of the level of the prolapse. Circumscribed spondylosis, developmental abnormalities, and vertebral shifts were present in 89 cases. In 61 instances the dorsal shift was 2 to 5 mm. There was flattening of the lumbar curve in 73.8 per cent of cases (321) and scoliosis in 56 per cent (244).

Myelography was performed in 326 cases. Narrowing of the intervertebral space was confirmed in 147 (50 per cent); definite prolapse with narrowing was demonstrated in 116 (39.4 per cent), and the surgical findings corresponded to the films in 201 cases (45 per cent).

It is concluded that plain films are of value in the diagnosis of disk prolapse and its differentiation from other vertebral disease and should precede myelography. Two tables.

### Absence of Motion at the Fourth and Fifth Lumbar Interspaces in Patients With and Without Low-Back Pain. Merrill C. Mensor and Gene Duvall. J. Bone & Joint Surg. 41-A: 1047-1054, September 1959. (490 Post St., San Francisco 2, Calif.)

Flexion and extension upright lateral roentgenograms of the lumbosacral spine were made in 527 consecutive patients with low-back pain and in a control group of 94 healthy individuals in an attempt to evaluate the significance of absence of motion at the fourth and fifth lumbar interspaces. Range of motion is not considered since normals for range have not been established. Presence or absence of motion is determined from the films by superimposing the sacrum on the two exposures and noting the difference in the angles formed at the lumbosacral junction. The fifth lumbar bodies are then superimposed and motion between the fifth and fourth vertebrae is determined in the same manner.

The 527 cases (393 in men and 134 in women) were separated into five clinical classifications for the purpose of analysis: A. *Sprains*; B. *Spondylosis, disk degeneration, or both*; C. *Lumbar intervertebral disk syndrome*; D. *Congenital anomalies*; E. *Miscellaneous*, including old fractures, postural defects, scoliosis, psychosomatic problems, etc. Patients were also grouped as to age and duration of symptoms. Symptoms of more than two months were classified as chronic, whereas, those of less than two months were considered acute.

Since the spine is able to compensate for restriction of motion in one area, it does not follow that loss of motion roentgenographically will be accompanied by a measurable loss on physical examination. Absence of motion at one or both of the two lower lumbar vertebrae was demonstrated in 226 of the authors' patients, but only a



small percentage of these showed clinical evidence of restriction. Limited motion occurred more frequently with symptoms of more than two months duration and in patients in the fourth, fifth, and sixth decades of life.

Absence of motion at the fourth and fifth lumbar vertebral levels was observed in 15 per cent of normal patients and in 43 per cent of patients complaining of low-back pain, without regard to etiological classification. Abnormal mobility, so-called primary instability, was seen in 8 per cent of normal controls and in 13 per cent of patients with symptoms. There is no definite evidence as to the cause of loss of mobility, but it is the authors' impression that changes in the periosteous soft tissues are responsible, rather than muscle spasm or degenerative changes.

Six charts.

JOHN F. RIESSER, M.D.  
Springfield, Ohio

**Blind Spots—First Rib Stresses—and the B. I. R. Presidential Address Delivered at the British Institute of Radiology on May 7, 1959.** J. Blair Hartley. *Brit. J. Radiol.* 32: 561-571, September 1959. (St. Mary's Hospitals, Manchester, England)

In his Presidential Address before the British Institute of Radiology, the author discusses his beliefs concerning abnormalities of the first ribs. In fairly full detail, he discusses the bony, vascular, and muscular anatomy of the thoracic inlet and first ribs in an effort to explain the mechanism of trauma to these structures. Because of the insertion of the scalene anterior muscle into the mid portion of the first rib, from the cervical spine, and the position of the clavicle immediately anterior to this muscle, trauma compressing the clavicle against the rib or stretching or pulling of the muscle, with motion of the head, can frequently cause a fracture. In complete fractures of the first rib, nonunion may be a common occurrence and this is more likely than a congenital synchondrosis. If the fracture is incomplete, union occurs.

The author does not believe that fatigue fractures of the first rib occur, for the following reasons. In young persons the rib cartilages anteriorly and posteriorly are pliable and insure an adequate "give" to stress. As the anterior cartilages later calcify, he states that an arthrodial joint appears between the anterior end of the bony rib and the calcifying cartilage, thus continuing pliability in this area.

The region of the first rib and its cartilage is designated "one of the diagnostic radiologist's blind spots." Among other blind spots the author mentions, but does not discuss at any length, diastematomyelia, ductus arteriosus, and radiological demonstration of the placental site. His final comment concerns the British Institute of Radiology, indicating that its main function is in the field of education.

Twelve roentgenograms; 8 diagrams.

LAURENCE B. LEINBACH, M.D.  
Bowman Gray School of Medicine

**Huge Osteoma of the Eleventh Left Rib.** Israel Steinberg. *J.A.M.A.* 170: 1921-1923, Aug. 15, 1959. (New York Hospital—Cornell Medical Center, New York, N. Y.)

A 3.5-pound osteoma had been attached to the eleventh rib of a 71-year-old man for fifty years but had caused no discomfort. Roentgenographic study showed it to contain calcium and bone, which readily established

the diagnosis of osteoma. The tumor was located in the gutter of the left pleural space, and produced roentgen findings simulating those due to a pulmonary mass. Despite its large size and displacement of the left kidney, the tumor remained benign; death was due to carcinoma of the right kidney.

Three roentgenograms; 1 photomicrograph; 1 photograph. MAJ. MARTIN A. THOMAS, M.C.  
MacDill Air Force Base, Fla.

**Transchondral Fractures (Osteochondritis Dissecans) of the Talus.** Albert L. Berndt and Michael Harty. *J. Bone & Joint Surg.* 41-A: 988-1020, September 1959. (M. H., Graduate School of Medicine, University of Pennsylvania, Philadelphia 4, Penna.)

Detached osteochondral fragments from the dome of the talus have been designated by a variety of terms. Loose bodies within joints have been ascribed to spontaneous necrosis; hence the term "osteochondritis dissecans." Clinically and experimentally, evidence indicates a traumatic etiology for these lesions as seen at the articular margin of the talus. The term *transchondral fracture* is suggested as being correct from both anatomical and etiological points of view. The definition given is "a fracture of the articular surface of a bone produced by a force transmitted from the articular surface of a contiguous bone, across the joint and through the articular cartilage to the subchondral trabeculae of the fractured bone."

A review of the literature yielded reports of 191 transchondral fractures of the talus, to which the authors add observations on 25 examples in 24 patients. Experimental work with 15 fresh above-the-knee amputation specimens elucidates the mechanism of production of these lesions.

Strong inversion of the dorsiflexed ankle will result in a transchondral fracture of the lateral border of the dome of the talus. Plantar flexion, inversion, and external rotation of the tibia on the talus will result in a fracture of the medial border, usually in the posterior half. This mechanism might be called rotational or torsional impaction.

The causative trauma may go unrecognized. The lesion itself may be painless, since the articular cartilage and bone have no nerve supply. Symptoms are due to associated ligamentous damage and soft-tissue swelling.

Roentgenographic diagnosis is paramount. The clinical findings are unreliable and many of these lesions will be regarded merely as severe sprains. Where symptoms of a sprain persist, roentgenographic examination with at least anteroposterior, oblique, and lateral views is mandatory. Long periods of immobilization appear to be necessary for proper healing when the fragment is undetached or partially detached. Detached or displaced fragments may necessitate surgical removal. Operative treatment will give better results than conservative management in both adults and children.

This report represents the abridgment of a thesis for the Master of Medical Science degree and is profusely illustrated and well documented, with a bibliography of 82 references. Those interested in orthopedic conditions might consult the original with profit. This type of investigation might be applied to other forms of "aseptic necrosis."

Twenty-two roentgenograms; 5 photomicrographs; 4 photographs; 6 diagrams; 1 graph; 5 tables.

JOHN F. RIESSER, M.D.  
Springfield, Ohio

Preliminary Study of the Shank Curve in the Normal Adult. Arthur L. ... 1976, September 20, N. Y. Measurements of roentgenograms with the subject's feet on a platform with the heels of the feet on a ... five different barefoot, but by shoe heels in Series 1, the heels of heights equal and 2. In the subject the heels, with the shoes. The measurement of the distal to the length of the slightly which either active shortening that observed in association of the foot of the foot articulation. If the heel to the heel significant mal Discomfort of bone is based on data to guide feet to vary ball relation a mathematical problems a motion shoe pose to correct the specific basis. One would large number of this study tive precautions. Four roentgenograms. Gas My Kleinberg. S2: 129-131, Stockholm, Sweden. The authors patients v and compared well as with expansive. It appears ment of the



**Preliminary Findings from a Roentgenographic Study of the Influence of Heel Height and Empirical Shank Curvature on Osteo-articular Relationships in the Normal Female Foot.** R. Plato Schwartz and Arthur L. Heath. *J. Bone & Joint Surg.* 41-A: 1065-1076, September 1959. (260 Crittenden Blvd., Rochester 20, N. Y.)

Measurements were made from a series of 65 lateral roentgenograms of the feet of two female subjects, (1) with the subject standing at ease barefoot and in shoes of five different heel heights, (2) with the subject standing barefoot, but with the heel of the foot supported only by shoe heels corresponding to those on the shoes used in Series 1, (3) with the subject standing barefoot with the heels elevated by voluntary muscle contraction to heights equivalent to the heel heights used in Series 1 and 2. Immediately after each exposure in Series 2, the subject was asked to remove the body weight from the heels, without removing the foot from light contact with the shoe heel, while a second exposure was made.

The measurements indicate that the length of the foot distal to the first metatarsal head does not change significantly as heel height is increased. The heel-to-ball length of the bare foot may or may not be shortened slightly when the subject stands with the heel raised either actively or passively. When shoes are worn, the shortening of heel-to-ball length may increase to twice that observed in the bare foot. This shortening occurs in association with elevation of the longitudinal arch of the foot by the shoe shank, accompanied by a hinging of the foot at the cuneonavicular and talonavicular articulations.

If the heel-to-ball design of a shoe does not correspond to the heel-to-ball shortening induced in the foot, significant malplacement of the foot in the shoe may occur. Discomfort, corns, and calluses, and eventually deformation of bone structures will result. Design of shoe lasts is based on empiricism since there are no quantitative data to guide model makers. The response of normal feet to various heel heights, shank curve, and heel-to-ball relationships has yet to be precisely determined on a mathematical basis. Until this is accomplished, foot problems arising from the use of improperly proportioned shoes cannot be eliminated. The authors propose to continue their studies in an attempt to define the specific relationships indicated on a mathematical basis.

[One wonders about the wisdom and safety of the large number of repeated x-ray exposures employed in this study on the two subjects and whether any protective precautions were taken—J. F. R.]

Four roentgenograms; 9 drawings; 4 tables.

JOHN F. RIESSER, M.D.  
Springfield, Ohio

### THE SPINAL CORD

**Gas Myelographic Studies in Syringomyelia.** Gösta Kleenberg and Georg-Fredrik Saltzman. *Acta radiol.* 52: 129-138, August 1959. (Serafimerlasarettet, Stockholm, Sweden)

The authors examined the gas myelograms of 28 patients with clinically characteristic syringomyelia, and compared these with 20 normal gas myelograms, as well as with observations in 9 cases with intramedullary expansive processes without signs of syringomyelia. It appeared that concomitant occurrence of enlargement of the cord with the atrophy distal to the enlarge-

ment is characteristic of syringomyelia. Syringomyelia with spinal cord enlargement but without atrophy could not be distinguished from an intramedullary expansive process of some other type.

Thirteen roentgenograms; 1 diagram; 1 table.

THEODORE E. KEATS, M.D.  
University of Missouri

**Spinal Epidural Hematomas. Experiences with Three Patients.** John J. Lowrey. *J. Neurosurg.* 16: 508-513, September 1959. (Department of Neurological Surgery, Straub Clinic, Honolulu, Hawaii)

Twenty-one previously recorded cases of spinal epidural hematomas unassociated with spinal fractures or a bleeding diathesis are listed and 3 new examples are reported. As in most of the cases from the literature, mild trauma or strain preceded the hemorrhage in these patients. Laminectomy and removal of clot was done in all 3 cases. Incomplete paralysis in 2 patients was followed by partial recovery of function; and complete paralysis in the third had persisted six months at the time of the report.

Roentgenograms of the spine were not helpful in this condition. Lumbar puncture showed anything from a complete block to normal dynamics. Spinal fluid levels of total protein ranged from normal to several hundred milligrams per cent. Myelography was the most useful procedure, but even this may be normal, as in 2 of the accumulated series of 24 cases.

One table.

EUGENE A. CORNELIUS, M.D.  
Houston, Texas

### GYNECOLOGY AND OBSTETRICS

**Lymphocysts: A Complication of Radical Pelvic Surgery.** Felix Rutledge, Gerald D. Dodd, Jr., and Filomeno B. Kasilag, Jr. *Am. J. Obst. & Gynec.* 77: 1165-1174, June 1959. (The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas)

The accumulation of fluid in the pelvic retroperitoneal space has been a serious complication following pelvic lymphadenectomy in the treatment of carcinoma of the uterus. The pool of lymph-like fluid produces varying pressure effects on the uterus, bladder, rectosigmoid, and blood vessels.

In a series of 281 patients undergoing lymphadenectomy, lymphocysts developed in 68. Analysis of the incidence of lymphocyst formation in relation to the stage of the carcinoma, preoperative irradiation, or metastases to the regional nodes revealed no one factor that could be isolated as the causative agent.

While the presence of the cystic mass could be confirmed by bimanual examination, the actual extent and significance of the collections were best appreciated by radiographic methods. Plain films alone are not reliable, however, since the normal pelvic soft-tissue shadows have been obliterated or distorted by the lymphadenectomy and only the presence of large lymphocysts can be appreciated without a contrast medium. Effects upon the urinary tract and colon are readily shown by pyelography and barium enema examinations.

The large and more incapacitating lymphocysts require drainage while the smaller, less distressing ones may be allowed to regress spontaneously. In all cases this complication produced prolonged postoperative disability.

During the past ten to fifteen years there has been

revival of interest in surgical treatment of carcinoma of the cervix and a large number of pelvic lymphadenectomies have been performed. Since this report is the second in the American literature dealing with lymphocysts following the latter procedure, it is possible that the incidence of this complication is substantially higher than has been recognized by the gynecologist or radiologist.

Eight roentgenograms; 7 tables.

ROBERT L. EGAN, M.D.  
University of Texas, Houston

**Radiographic Demonstration of Uterine Developmental Abnormality as a Cause of Abnormal Lie of the Fetus.** M. G. F. Donnan. M. J. Australia 2: 402-403, Sept. 19, 1959. (King Edward Memorial Hospital, Perth, Western Australia)

Two cases are reported in which the upper border of the pregnant uterus was seen to be concave instead of convex, with the fetus lying transversely. At cesarean section the radiographic impression of subseptate uterus was confirmed.

Two roentgenograms; 3 diagrams.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**The Etiology, Development, and the Effect upon Pregnancy of Protrusio Acetabuli (Otto Pelvis).** H. H. Francis. Surg., Gynec. & Obst. 109: 295-308, September 1959. (Liverpool University, Liverpool, England)

During the past five years, 5 cases of primary acetabular protrusion (Otto pelvis) were recognized in women attending Liverpool Maternity Hospital and Mill Road Maternity Hospital, Liverpool. A sixth case was found in the gynecology ward.

Primary acetabular protrusion is of two types, osteoasthenic and osteoarthritic. The former is characterized by rapid development at puberty, becoming static in a few years. No change is seen in the femoral head but secondary osteoarthritis may develop in middle life. In the osteoarthritic variety, the acetabulum, joint cavity, and femoral head show osteosclerosis and osteophytes at an abnormally early age. Protrusion commences at puberty and may progress throughout life.

X-ray examination in the osteoasthenic type shows that the protrusion involves all arcs of the acetabulum. Because of the regularity and symmetry of the acetabular outlines and the relative absence of osteoarthritis the protrusion is frequently overlooked. The roentgenographic appearances in the osteoarthritic type vary from case to case. The curve of the acetabulum tends to be irregular, the protrusion most often being maximal in the superomedial quadrant. The bony outlines lack the bilateral symmetry of the osteoasthenic type. The joint space is irregularly narrowed and osteophytes are common. The head of the femur shows moderate distortion, especially flattening of its upper surface, together with osteosclerosis and subchondral cyst formation.

A reduction in range of hip motion is a common sign and makes the lithotomy position difficult. The forepart of the pelvis is narrow, interfering with engagement of the fetal head so that an increased incidence of persistent occipito-posterior positions and face presentations results. Obstructed labor has not been recorded as being caused by protrusio acetabuli alone.

Roentgenographic demonstration of acetabular pro-

trusion in 6 relatives of one of the author's patients establishes the fact that primary osteoasthenic protrusion is genetically determined.

Seventeen roentgenograms; 1 diagram; 1 chart; 1 table.

DAVID RITCHIE, M.D.  
University of Pennsylvania

## THE GENITOURINARY SYSTEM

**On the Application of Tomography to Urologic Roentgenology.** E. Hajós. Fortschr. a. d. Geb. d. Röntgenstrahlen 91: 366-382, September 1959. (In German) (Medizinische Universität, Budapest, Hungary)

Tomography is used almost routinely in retroperitoneal pneumography and renal arteriography. It is employed less frequently in excretory urography, although the combined procedure yields sufficient information to make retroperitoneal insufflation unnecessary in most instances.

In order to decrease lumbar lordosis, the examination is carried out with the patient in the supine position, with lower extremities elevated and the knees flexed. Several tomographic sections are required to demonstrate the entire kidney; for the enlarged kidney additional levels are essential. In the thin patient the fulcrum is set at 6-7 cm., in the average patient at 7-8 cm., and in the very obese at 8-10 cm.

With tomography, calcifications overlying the renal shadows can be localized exactly. If a calcification is seen distinctly at the level of the kidney, it lies within the kidney. In the pyelogram calculi in the collecting system may be obscured by the contrast medium. By superimposing tomograms taken prior to pyelography on these pyelograms, the exact position of the calcification within the collecting system can be determined. Tomography is also of value in the demonstration of hypoplastic and malformed kidneys and in tumors of the kidney and surrounding retroperitoneal structures. In examination of the collecting system, it can be used with either excretory or retrograde pyelography. Since the collecting system does not lie in a horizontal plane, sections of several layers are necessary. The renal pelvis usually lies more ventrally than the calyces. In hydronephrosis the entire collecting system is displaced anteriorly. In horseshoe kidney, the position of the lower calyces is far anterior. The procedure is especially helpful in the diagnosis of renal calculi and in tuberculosis of the kidney.

Normally the ureter lies most ventrally at about the level of L-4; its course from this point is in both directions dorsally. Parts of the ureters hidden by the transverse processes or by the contrast-filled bladder are clearly seen on tomograms; even in nonobscured areas a small calculus may be identified only by this means.

The author cautions against the use of too much contrast material in examination of the urinary bladder, since tomography cannot blur large dense areas. The injection of gas around the bladder filled with contrast medium permits good visualization of the bladder wall and is particularly useful in tumors of the wall and in diverticula.

By means of tomography, calcification in the prostate can be distinguished from the overlying symphysis. Tomography of the seminal vesicles may disclose pathological changes not otherwise demonstrated.

Twenty-eight roentgenograms.

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Manuel Vi-  
255-272, M-  
(In Spanis-  
Cuba)

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**Nephrocalcinosis: A Clinico-Radiological Study.**

Manuel Viamonte Puncet. *Rev. cubana de pediat.* 31: 255-272, May; 361-376, July; 415-450, August 1959. (In Spanish) (Universidad de La Habana, Habana, Cuba)

In what the author believes is the first clinico-radiological study of nephrocalcinosis in Cuba, 14 cases are reported. Of these, 13 were demonstrated roentgenologically and 1 was discovered at autopsy. The condition was considered to be due to primary hyperparathyroidism in 3 cases (21.43 per cent); and to chronic pyelonephritis in 3 (21.43 per cent); in 1 case (7 per cent) it was associated with secondary hyperparathyroidism, and in 1 (7 per cent) with sarcoidosis. No etiology was established in 6 patients (42.85 per cent).

Renal calcifications may be homogeneous or heterogeneous. Radiologically there are three types: cortical, medullary, and corticomedullary. A provisional etiologic diagnosis can occasionally be made from analysis of the type and distribution of the calcium deposits. In most instances blood chemistry and urinalysis permit the correct diagnosis.

Nephrocalcinosis does not mean a hopeless situation: its detection should be followed by a thorough clinical study, as in some cases the calcification is reversible or its progress can be arrested. Treatment is primarily etiological. It is suggested that some modifying factors of the connective-tissue ground substance, such as desoxycorticosterone acetate, may prevent further progression of the calcification.

Thirty-five roentgenograms; 2 photomicrographs; 3 diagrams; 11 tables.

**THE ADRENALS**

**Idiopathic Adrenal Calcification in Infants and Children.** J. Luther Jarvis and William B. Seaman. *Am. J. Roentgenol.* 82: 510-520, September 1959. (Columbia-Presbyterian Medical Center, New York 32, N.Y.)

Calcification of the adrenal gland has been found in association with tuberculosis, Addison's disease, Niemann-Pick's disease, cysts, adrenal hemorrhage, and adrenal neoplasm (carcinoma, neuroblastoma, pheochromocytoma, and ganglioneuroma). It occurs also in infants without any apparent adrenal disease. Twenty-six cases of such idiopathic calcification are reported here.

In this series of 26 cases there were 17 males and 9 females, ranging from five days to twelve years of age. In 19, calcification was an incidental roentgen discovery. Seven additional cases were revealed at necropsy. Necropsies were also performed on 3 of the 19 patients in whom a roentgen diagnosis was made.

In 14 cases, clinical follow-up ranged from three to twenty years without any evidence of adrenal disease. In 2 (of the 19) the adrenal calcification had been noted only recently. The other 3 died shortly after the discovery of the calcification. Sixteen had negative cutaneous tuberculin tests and in 2 no tuberculin test was performed. One patient with a positive tuberculin test was found at necropsy to have pulmonary but no adrenal tuberculosis.

Calcification was bilateral in 10 of the 19 cases. It was usually apparent as irregular, discrete densities grouped in triangular fashion.

Four of the 10 children coming to necropsy had roentgen examination during life. Adrenal calcification was

seen in 3. The fourth had calcification in a microscopic cortical adenoma. In 2 premature infants there was microscopic calcification. In another instance calcification was found in an aberrant pelvic adrenal gland. None of this group had clinical signs of adrenal insufficiency or evidence of tuberculosis with the exception noted above.

Calcareous deposits usually occurred in the inner portion of the cortex and medulla. The preservation of the outer cortical layers may explain the lack of adrenal insufficiency.

Adrenal calcifications must be differentiated from calcification in gallstones, lymph nodes, costal cartilages, and arteries. If calcification is unilateral, adrenal neoplasm must be considered. Neuroblastoma is the most frequently encountered calcified tumor of infancy and childhood (50 per cent). If there is a mass with adrenal calcification, neuroblastoma is the most likely diagnosis. Adrenal calcification without a mass makes idiopathic adrenal calcification more likely. Adrenocortical carcinoma is usually associated with Cushing's disease or adrenogenital syndrome. Pheochromocytoma is uncommon in children. In 3 cases of adrenal calcification in Niemann-Pick's disease, the calcification was massive and limited to the medulla. Addison's disease is rare in childhood.

Trauma and hemorrhage as a cause of adrenal calcification are emphasized. In 22 of 26 patients in the present series, there was an abnormal obstetrical history, including forceps delivery, prematurity, breech delivery, and excessive size (over 9 lb.). Anoxia is also implicated as a possible cause of adrenal hemorrhage.

Eleven roentgenograms; 6 tables.

MICHAEL LAZOREK, M.D.

St. Vincent's Hospital, New York, N.Y.

**TECHNIC**

**The Dynapulse Method of Ultrashort (Millisecond) Timing and Improved Rapid Impulse Timing in Medical Roentgenography.** Robert B. Funch. *Am. J. Roentgenol.* 82: 423-432, September 1959. (Germantown Hospital, Philadelphia 44, Penna.)

Exposure requirements are critical in angiocardiology for production of sharp images and elimination of the blur of motion, and faster timing than is obtainable with conventional roentgen-ray equipment is desirable. Conventional equipment operating from a 60-cycle power supply usually produces its shortest exposure at 1/60 second. Half-cycle exposures of 1/120 second are possible with the use of an impulse timer, but this is the shortest exposure limit that can be accomplished without raising the frequency of the power-line supply. With a Dynapulse timer, exposures of 1/2,000 second to 5 milliseconds can be obtained. This timer, rather than employing a mechanical switch, makes and breaks the circuit in the secondary circuit of the high-tension transformer, using a controlled electron-flow vacuum tube as a contactor.

Comparative tests of radiographic sharpness of moving mechanical test objects subjected to 1/120 second and 1/1,000 second exposures revealed the motion to be "stopped" only by the more rapid exposure. In ordinary radiography, where no motion is encountered, no difference was found in the roentgen detail when these two exposures were used. In angiocardiology, the image is believed to be sharper at exposure levels exceeding 1/60 of a second, but no radiographic superiority

was discernible between the 1/120 second and 1/1,000 second angiocardigrams. In aortography and cerebral angiography, no diagnostic advantage of millisecond timing over conventional methods was apparent. A side development of the Dynapulse method, however, has been the reduction in radiation exposure to the subject.

Seventeen roentgenograms; 1 diagram.

JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Experiences with Retroperitoneal Air Insufflation (Retropneumoperitoneum).** E. Sövényi. *Radiol. clin.* 28: 198-211, July 1959. (In German) (I. Medizinalwissenschaftliche Klinik der Universität, Szeged, Hungary)

Presacrally injected air shows homogeneous distribution in the entire retroperitoneum, outlining the kidneys, adrenals, psoas margins, liver, spleen, and sometimes the large and small intestines, vena cava, and abdominal aorta. The pancreas is not demonstrated because the air cannot enter the peripancreatic space. Perirenal air insufflation must be done for each side separately. Since the retroperitoneal space communicates with the openings in the diaphragm, with the mediastinum, and with the suprapleural loose connective tissue up to the deep neck muscles, the injected air can sometimes be localized in these regions. The site of injection is the relatively avascular presacral region and the injection is made either 1 cm. above the sacrococcygeal joint or through the anococcygeal ligament. The latter method was used by the author. Oxygen, carbon dioxide, or air is employed as the contrast medium. The oxygen is absorbed in twenty-four hours, carbon dioxide in three days, and air in four to five days.

Retropneumoperitoneum is contraindicated in the presence of circulatory and coagulation disturbances and in acute abdominal disease. The most dangerous complication of the procedure is air embolism; in such cases the left lateral decubitus position could be lifesaving.

At the author's clinic, 62 patients have been examined by retropneumoperitoneum since 1953, with no appreciable side-reactions. In many cases the examinations were supplemented by retrograde pyelography and tomography. Abnormalities of the kidneys, adrenals, pancreas, and spleen were found in 24 cases.

When a tumor of the adrenals was suspected and the organs were not adequately visualized on the routine films, a sagittal tomogram was made. In the author's experience, the size of the adrenals can be almost def-

initely appraised on cuts of 1 cm. Normally, the adrenals are of various sizes. The right is triangular and adheres loosely to the upper pole of the kidney. The left is crescent-shaped and lies more medially, adhering tightly to the kidney. Enlargement of one or the other adrenal can be simulated by a malignant tumor of the upper portion of the kidneys, shadows of the fatty tissues, the right lobe of the liver, the spleen, and also by fluid in the gastric fundus.

Hyperfunction of the adrenal cortex can cause enlargement of the organ, but while the shadow can be more massive, morphological changes are usually not visualized. Tumors of the medulla cause morphological changes, and the organ is always enlarged and its outline irregular.

Air in the retroperitoneum shows the outline, position, and enlargement of the kidneys. When renal disease was suspected an intravenous pyelogram and additional retrograde studies and tomograms were obtained. For the diagnosis of congenital lesions of the kidneys, if other methods fail, retropneumoperitoneum is helpful.

Pancreatic abnormalities can be demonstrated only by lateral films and lateral sagittal tomograms. Space-occupying lesions of the retroperitoneum are usually not demonstrable due to the infiltration of surrounding tissues which do not allow the entry of air. The smooth, well defined outline of a retroperitoneal tumor points to a benign process.

The author believes that for the demonstration of the retroperitoneal space air is best, because of its slower absorption; the examination, sometimes even days later, can be supplemented with retrograde tomograms, splenoportography, etc.

Nine roentgenograms. ILONA D. SCOTT, M.D.  
Lewisburg, W. Va.

**Method for Direct Copy of Radiographs.** Herman Wechsler, Bernard Rapoport, and David Lubin. *J. Urol.* 82: 400-401, September 1959. (VA Hospital, Bronx 68, N. Y.)

The authors describe a simple and inexpensive method of copying radiographs. The film to be reproduced is placed upon an x-ray illuminator with fluorescent lamps and covered with an unexposed film held firmly in place for 45 seconds for Eastman Blue Brand film and 90 seconds for Dupont film. The film is then developed in the usual manner. If less density is desired in the finished copy, it is necessary to increase the exposure time.

JOSEPH M. WINSTON, M.D.  
University of Pennsylvania

## RADIOTHERAPY

**New Horizons in Radiotherapy of Malignant Disease.** Henry S. Kaplan. *J.A.M.A.* 171: 133-138, Sept. 12, 1959. (Stanford University Medical Center, Palo Alto, Calif.)

This article is one of general interest with notation of recent medical discoveries and recently developed technics which seem to offer promise for the future radiotherapeutic management of malignant disease. Comment is made on the availability of new sources of high-energy radiations and methods of more precise dosimetry. Developments in the understanding of cellular radiobiology may lead the way to favorable practical results. Mentioned in this connection are

new methods of cell culture which may allow estimation of radiosensitivity of different groups and classes of cells, with possible later development of a rational procedure for determining the response of specific human tumors. Studies in cell oxygenation in normal and in tumor tissues may permit development of methods to increase radiosensitivity of malignant tissues. Further possibilities include the use of chemical agents to render tumor cells more radiosensitive.

Of considerable interest is the mention of the problem of centralization of radiotherapy care for patients with radiocurable cancer. "Although palliative therapy can be carried out satisfactorily by most general

radiologists, therapy centered in radiocurable cancer centers staffed by their practicing radiologists, supporting arguments of many of them need for and various technical Three roentgenograms.

Leiomyosarcomas. *Ellen J.A.M.A.* 171: The Henry I. The author of the uterus in primary tumor thirty-two years old pain and tumor completely removed the operation dose of 720 After eighteen to limp because of examination of left femur palpable in tumorous pyelogram with deformity large tumor Biopsy material kidney was removed uterus removed About one developed, and found. Aggravated to that of the femur good results. home, having tumors of the Four roentgenograms photograph.

Primary Malignant R. Freund, Am. J. Obs. (Episcopal Hospital) The author of melanoma of reported cases women; both Because of surgery, of 6,000 r each instance metastases 6 months. Treatment of excision of node dissect



radiologists, the experience of many European radiotherapy centers indicates that the patient with radio-curable cancer has the best chance for cure in cancer centers staffed by well trained physicians who limit their practice to full time radiotherapy." As a supporting argument the author notes the very high cost of many of the newer high-energy radiation sources, the need for ancillary services, including radiologic physicists, and the importance of careful comparison of various technics with regard to end results.

Three roentgenograms; 2 photographs; 1 chart; 1 table.  
JAMES W. BARBER, M.D.  
Cheyenne, Wyo.

**Leiomyosarcoma of the Uterus with Unusual Metastases.** Ellery T. Drake and Glen D. Dobben. *J.A.M.A.* 170: 1294-1298, July 11, 1959. (G. D. D., The Henry Ford Hospital, Detroit 2, Mich.)

The authors report recurrence of a leiomyosarcoma of the uterus eighteen years after complete removal of the primary tumor. When originally seen, the patient was thirty-two years old. She complained of lower abdominal pain and a large pelvic mass was palpable. At operation a tumor measuring 18 cm. in diameter was completely removed without difficulty. Two weeks after the operation "deep x-ray therapy" was given (skin dose of 720 r to the pelvis on four successive days). After eighteen years of good health, the patient began to limp because of pain in the left thigh. Roentgen examination disclosed bone destruction in the left femur with pathological fracture. A mass was palpable in the left side of the abdomen. An intravenous pyelogram showed this to involve the left kidney, with deformity of the collecting system. At operation a large tumor was found in the left retroperitoneal region. Biopsy material from the femur as well as from the kidney was histologically similar to tissue from the uterus removed at the original operation.

About one year later proptosis of the right eye developed, and at operation a retro-orbital tumor was found. Again the microscopic appearance was similar to that of the original tumor. Palliative x-ray therapy to the femur as well as to the abdomen was given with good results. The patient subsequently died quietly at home, having survived three years after onset of symptoms of the terminal illness. There was no autopsy.

Four roentgenograms; 4 photomicrographs; 1 photograph.  
D. D. ROSENFELD, M.D.  
Los Angeles, Calif.

**Primary Malignant Melanoma of the Vagina.** Donald R. Freund, Eugene E. Kegel, and John H. Dugger. *Am. J. Obst. & Gynec.* 78: 290-294, August 1959. (Episcopal Hospital, Philadelphia, Penna.)

The authors present 2 cases of primary malignant melanoma of the vagina, bringing the total number of reported cases to 30. Both patients were elderly white women; both sought medical aid for vaginal bleeding.

Because of poor cardiovascular status, contraindicating surgery, treatment was with Co<sup>60</sup>. A tumor dose of 6,000 r caused regression of the primary tumor in each instance and stopped the vaginal bleeding, but metastases developed with death ensuing within seven months.

Treatment is controversial, but surgery with wide excision of the primary lesion with or without lymph node dissection is generally recommended. Death,

however, usually occurs within a year. One patient is said to have survived fifteen years in spite of local recurrence four years after original treatment (Mino *et al.*: *Am. J. Obst. & Gynec.* 56: 325, 1948).

A complete list of references is included.

Two photomicrographs. ROBERT L. EGAN, M.D.  
University of Texas, Houston

**Sacroccygeal and Vertebral Chordomas and Their Treatment.** Hugo Rosenqvist and Georg-Fredrik Saltzman. *Acta radiol.* 52: 177-193, September 1959. (Radiumhemmet, Stockholm, Sweden)

Chordomas are difficult to treat. Not one in a series of 200 collected cases could be reported as cured, though some showed long control periods which may have been due to the naturally slow growth of this neoplasm. These tumors are believed to arise from remnants of the notochord and occur most commonly in the midline, in the sacrum (50 per cent), base of the skull (40 per cent), and rarely in the vertebrae. They are generally considered to be radioresistant.

The authors report 16 cases. Trauma as a causative factor was discounted in 7 cases because the time period varied from months to years. The case histories extended from six months to seven years. Though metastases are said to be unusual (10 per cent of all cases), they were clinically established in 3 of the present series, being proved histologically in 1.

All but 1 patient in this group received roentgen therapy. Ten were treated also by surgery. In general, irradiation was given at 170 kv, in total dosage of 2,500 to 3,200 r. Repeated series were used in some instances. Two patients had recently received telegamma arc therapy, with cobalt 60, following recurrence of symptoms after earlier roentgen therapy.

The effect of radiotherapy alone could be assessed in 7 cases. Complete or very satisfactory alleviation of pain was achieved in all of these, and all tumors except one definitely decreased in size, but in no instance was a curative effect obtained.

Preoperative irradiation was given in one case—about 3,500 r to the center of the tumor in eighteen days. Operation was performed ten weeks later but was not histologically radical. Recurrence developed in eighteen months. Effects of postoperative irradiation were difficult to assess, but this form of treatment is not considered to have been "particularly attractive." Supervoltage therapy appears promising, but the proximity of the rectum and spinal cord in many instances calls for extreme caution in depth dose determinations.

Sixteen case reports, brief and interesting.

One diagram. JESSHILL LOVE, M.D.  
Santa Barbara, Calif.

**The Use of the Rad in Clinical Practice: A Contribution to a Symposium at the British Institute of Radiology, November 20, 1958.** C. W. Wilson. *Brit. J. Radiol.* 32: 584-586, September 1959. (Westminster Hospital, London, S. W. 1, London, England). D. E. A. Jones. *Brit. J. Radiol.* 32: 586-587, September 1959. (Mount Vernon Hospital and the Radium Institute, Northwood, Middlesex, England). F. Ellis. *Brit. J. Radiol.* 32: 588-595, September 1959. (Churchill Hospital, Oxford, England)

The three authors whose names appear above contributed to a symposium presenting different ideas as to the use of the rad as a unit of radiation dose.

Wilson classifies himself among the "reluctants"



who feel that the universal acceptance of the rad in clinical practice would only add further "ambiguities" to an already ambiguous situation. He feels that in the light of our present knowledge, we are not able to say exactly what is the biologically and clinically significant absorbed dose in all cases. Reasons for this attitude in view of the wide range of modalities employed in radiotherapy are offered.

Included in the paper is a useful table which provides an outline of the rad equivalent to 1,000 r for various therapeutic electromagnetic radiations for muscle, fat, bone (average), and compact bone. The values presented are based upon measured energy and absorption data which were determined in 1946. The author uses this table in his own therapy center.

One table.

GEORGE C. BARRETT, M.D.  
Bowman Gray School of Medicine

Jones had made a limited survey, on behalf of the Scientific Subcommittee of the Hospital Physicists' Association, of the use of roentgen/rad conversion factors at some of the larger British radiotherapy centers. His conclusion was that, for the time being, exposure dose was likely to be a much more satisfactory basis for comparison than the use of the rad, particularly for conventional x-ray qualities and for bone and its soft-tissue components.

With respect to soft tissues, with the possible exception of fat, acceptable conversion factors may be calculated to two significant figures for all photon energies presently of clinical importance. The problem is much greater in regard to bone and is not yet solved. There are several sources of uncertainty, including the difference between conversion factors for bone tissue proper and for the soft tissue contained within bone. This difference in factors increases with reduction in energy of the primary beam. In addition, there is a factor of change in quality of the beam with increasing depth in the tissues. Because of the various physical, biochemical, and other factors which enter into the eventual biological effect of a given beam on a given tissue,

it is felt to be premature at the present state of our knowledge to go over to the rad as a unit for clinical dosage in conventional roentgen therapy.

The use of the rad in the determination of soft-tissue dose in isotope beta-ray therapy is of advantage, however, since the absorbed energy can usually be evaluated with accuracy. There is also something in favor of the rad for high-energy gamma and x-ray beams, since the incident dose cannot be expressed in roentgens and the range of uncertainty in the case of bone is greatly diminished.

The conclusion is that it is far better to appreciate the practical meaning of the roentgen than to adopt a new unit which is "of little clinical significance" at present.

DAMON D. BLAKE, M.D.  
Bowman Gray School of Medicine

Ellis believes that the rad should be accepted as the preferred unit for stating dose and presents an excellent case in its favor by pointing out that only by its adoption can different centers accurately compare their cases. A given physical dose expressed in rads and delivered with the proper time dose relationship should produce the same biological effect in all centers that use radiation therapy. While the variables that may enter into the calculation of dosage cannot be completely eliminated, they can be better controlled by standardization of techniques for dose measurement and of dosage calculations. It is pointed out that only through the use of rads can summation of dosage from different radiations be carried out. The relative biological effect must, of course, be considered in this.

A further argument for the use of the rad is the fact that it has been endorsed by the I.C.R.U.

Several charts and graphs accompany this contribution, the one of greatest interest being Table II, which depicts the energy absorption for various radiative qualities in different scattering media.

Seven figures; 5 tables.

WALTER E. DEYTON, M.D.  
Bowman Gray School of Medicine

## RADIOISOTOPES

**Use of Radioactive Iodine in the Diagnosis of Thyroid Disorders.** A. W. G. Goolden. *Brit. M. Bull.* 16: 105-112, May 1960. (Hammersmith Hospital, London, England)

The problems involved in the interpretation of the results of  $I^{131}$  tests are discussed in some detail. In practice, difficulties arise in only a small proportion of the patients studied.  $I^{131}$  tests are on the whole very satisfactory for detecting hyperthyroidism and are particularly helpful in patients with thyrocardiac disease with few of the signs or symptoms of thyrotoxicosis.

It is unreasonable to expect that any  $I^{131}$  test will distinguish every patient as being either euthyroid or hyperthyroid. Clinical experience shows that there is no sharp transition between these states. In doubtful cases the diagnosis is usually resolved by observing whether there is any response to treatment with an antithyroid drug.

In the diagnosis of hyperthyroidism, early or intermediate estimations of thyroid uptake and  $PBI^{131}$  tests appear to be equally reliable. An early uptake test, although requiring an intravenous injection, is convenient

for the patient and is completed within half an hour. An excretion test as the T index (Fraser *et al.* *Quart. J. Med.* 22: 99, 1953), though less convenient for the patient, compares favorably with other tests provided that accurate collection of urine is ensured, but results are sometimes invalidated because of incomplete collection. In the diagnosis of hypothyroidism an excretion test is usually more reliable than other  $I^{131}$  tests.

As a general rule, an uptake test employed in conjunction with a  $PBI^{131}$  test is the most satisfactory method of assessing thyroid function. The combination of a high uptake and a high  $PBI^{131}$  value is nearly always due to thyrotoxicosis. A suppression test with tri-iodothyronine may be used if further confirmation is needed. Patients who have been treated with  $I^{131}$  are less easily assessed, since the  $PBI^{131}$  is of no diagnostic value, and a high uptake may occasionally persist despite a return to the euthyroid state.

Two figures; 1 table.

[This is one of 15 papers comprising a symposium on The Thyroid Gland by 20 British authorities who are conducting original work. For the most part they de-

scribe the research they themselves have been carrying out, as well as reviewing and evaluating research being conducted in other countries.]

**Use of  $^{131}\text{I}$ -Labelled Fat in the Study of Lipid Handling in Patients with Coronary Artery Disease.** Robert H. Sellar, Jonas Brachfeld, Herschel Sandberg, and Samuel Bellet. *Am. J. Med.* 27: 231-240, August 1959. (Philadelphia General Hospital, Philadelphia 40, Penna.)

For a study of the handling or disposition of lipid in patients with coronary artery disease, 51 normotensive men between the ages of nineteen and fifty-three (20 "normal" subjects; 21 with documented previous myocardial infarction; 10 patients with abnormalities but no evidence of infarction) were given a test meal containing a small amount of radioactive  $^{131}\text{I}$ -labeled glyceryl trioleate. Serial blood samples were drawn after ingestion of the isotope to determine the total circulating radioactivity contained in the whole blood and in the trichloroacetic acid precipitable fraction. This was reported as percentage of ingested dose.

At peak time and at twenty-four hours, the differences between the mean levels of radioactivity obtained in the control group and those in the group with myocardial infarction were statistically highly significant ( $p < 0.0005$ ). There was little overlap and a high degree of separation. An abnormal response to the test was demonstrated in every patient who had had myocardial infarction, although many in this group had normal serum levels of cholesterol, lipid phosphorus, and alpha and beta lipoproteins. There was no significant relationship between test values and age or weight.

The results of the test in the 10 patients with abnormalities such as hypercholesteremia, marked obesity, and intermittent claudication, are also presented.

The clinical significance and possible applications of the test are discussed.

Two figures; 6 tables.

**Surface Back-Scatter for Rectangular Fields in the Quality Range from a Half-Value Layer of 1 mm. of Al to Cobalt 60 Gamma Radiation.** M. L. Emmett. *Brit. J. Radiol.* 32: 615-616, September 1959. (Bristol Royal Hospital, Bristol, England)

In order to obtain the skin dose rate with a particular applicator the air dose must be multiplied by the surface backscatter factor, which depends on the quality of the radiation as well as the size and shape of the irradiated field. The author points out that there are no data available for elongated fields in the half-value range of 1 to 8 mm. Al or for cobalt-60 radiation and that values for the range of 1 to 5 mm. Cu must be calculated by use of the elongation correction graph of Jones.

The author relates that there is a similarity in the graphs representing the relation between area and scatter (expressed as a percentage of the primary beam at the surface) for the above radiations. Further he shows that for each of these qualities and depths, if the percentage scatter is multiplied by a factor,  $F_s$ , and the area multiplied by another factor,  $F_a$ , the area scatter graphs become almost identical (a table of  $F_s$  and  $F_a$  for the above qualities is included). Thus the scatter at the centers of rectangular fields for a particular half-value layer and depth may be easily converted to give similar information for any half-value layer and depth.

Two figures; 1 table. RICHARD L. WITCORSKI  
Bowman Gray School of Medicine

**Disseminated Demyelination of the Brain Following  $\text{Co}^{60}$  (Gamma) Radiation.** P. Lampert, M. I. Tom, and W. D. Rider. *Arch. Path.* 68: 322-330, September 1959. (Division of Neuropathology, University of Toronto, Toronto 5, Ont., Canada)

A case of delayed demyelination and necrosis of the brain following  $\text{Co}^{60}$  irradiation is reported. In March 1953, a basal-cell carcinoma was removed from the left external auditory canal of a 32-year-old woman. Post-operatively the external canal was treated by means of a radium applicator, a surface dose of 1,000 r being delivered in a period of forty-five minutes. For three years the ear remained normal. Pain and discharge from the ear then developed and a fleshy mass could be seen filling in the canal. A left radical mastoidectomy was performed in February 1956; histologic examination of the specimen showed recurrent basal-cell carcinoma. By August 1957, the recurring tumor had spread to involve the tragus and preauricular region. From Aug. 29 to Sept. 26, 1957, the patient was treated with  $\text{Co}^{60}$  through a single  $6 \times 6$ -cm. field directly over the left ear. A tumor dose of 5,000 r in a period of four weeks was believed safe and, at the same time, tumor-lethal. The depth of the tumor was considered to be 3 cm. (87 per cent depth dose). Physical factors were: h.v. l. 11 mm. Pb; dose rate, 34.97 r/min.; 20 treatments in twenty-nine days; daily dose 288 r, to a given maximum of 5,750 r (100 per cent).

On Dec. 12, 1957, the patient was admitted to the hospital with a two-week history of blurred vision, followed by diplopia, nausea, and vomiting; she also complained of slurred speech and difficulty in walking and swallowing. Recurrent tumor within the posterior cranial fossa was considered to be the most probable explanation for the clinical state, but ventriculography on Dec. 17 disclosed no abnormality. The same day the patient became akinetic and mute. She remained in decerebrate rigidity until her death on Dec. 27. Postmortem examination of the brain revealed disseminated plaques of demyelination with central necrosis and occasional petechial hemorrhages. These areas were strictly within the beam of  $\text{Co}^{60}$  and more numerous closer to the source of radiation. The lesions could not be explained on an ischemic basis secondary to degenerative and obliterative changes of the blood vessels.

The possibility of an autoimmune reaction localized to the irradiated brain tissue is discussed.

Eight figures.

**Cancer Palliation. Extracorporeal Pump Perfusion of Radioactive Isotopes and Nitrogen Mustard as Adjuncts to External Radiation Therapy.** Robert C. Hickey, Charles A. Johnson, Titus C. Evans, and David Alftine. *Arch. Surg.* 79: 416-426, September 1959. (State University of Iowa College of Medicine, Iowa City, Iowa)

An attempt was made to perfuse a localized body segment with an extracorporeal pump in an effort to assess the delivery of cancericidal materials to such a segment. Five human subjects with various types of lower extremity neoplasms were thus treated. In every instance the distal superficial femoral artery and vein were cannulated above the knee with polyethylene catheters which were attached to a pump which was used for circuit perfusion through the extremity. A tourniquet was applied above the segment in an attempt to localize the perfusions to the area and to prevent

systemic contamination with the perfused material. The pump system was filled with 400 ml. of heparinized isotonic solution to which nitrogen mustard was added, as well as radioactive phosphorus ( $P^{32}$ ) or radioactive gold ( $Au^{199}$ ). During the same period roentgen therapy or cobalt ( $Co^{60}$ ) teletherapy was given.

Although the patients suffered from a variety of malignant lesions and the controls were complicated because of the complexities of the therapy, the authors received some clinical impressions. They believe that  $P^{32}$  and  $Au^{199}$  are potentially hazardous for use in therapeutic amounts. They thought that there were some salutary effects from perfusion of nitrogen mustard with external irradiation given during the same period. They were sufficiently encouraged to think that further trials with an extracorporeal pump for localized perfusion are justified.

Eight figures.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Liver Blood Flow in Man; Studies Utilizing Radioactive Colloid. I. Normal Values.** George L. Nardi, Hugo M. Palazzi, and Marie-Louise Levy. *Gastroenterology* 37: 295-298, September 1959. (Massachusetts General Hospital, Boston 14, Mass.)

Hepatic hemodynamics were studied in 21 normal subjects with  $P^{32}$ -tagged chromic phosphate. Two to four microcuries of the radioactive compound were injected intravenously, and heparinized blood samples were then withdrawn after two, three, four, six, eight and ten minutes for counting. Counts per minute were plotted on semilogarithmic paper as a function of time and the best straight line was fitted to the points. The slope of this line represents the fraction of the patient's blood volume perfusing the liver per unit time and has been termed the colloid disappearance rate constant,  $K$ . Blood volume determinations were done simultaneously by combining blue dye with the isotope.  $K$  multiplied

by the blood volume gives the liver blood flow in liters per minute. Normal values of 1,400 c.c. per minute in women and 1,600 c.c. per minute in men were established.

This paper presents the authors' technique and calculations in detail and should be read in the original by those planning to study hepatic hemodynamics by the isotope method.

One table.

MAJ. MARTIN A. THOMAS, M.C.  
MacDill AFB, Tampa, Fla.

**Dynamics of Bone Healing and its Effect on the Skeletal System in Vivo Using Strontium<sup>85</sup> and Calcium<sup>45</sup>.** H. Koenig and John H. Heller. *Surg., Gynec. & Obst.* 109: 351-354, September 1959. (New England Institute for Medical Research, Ridgefield, Conn.)

Strontium 85 and calcium 47 can be used interchangeably to measure the dynamics of bone healing in manually induced fractures between the head and shaft of the tibia of test rats. Because of its availability  $Sr^{85}Cl_2$  was used in the experiments reported here. It was injected subcutaneously and the uptake measured with a gamma ray spectrometer.

Immediately after fracture there is a loss of mineral not only from the fracture site, but from the entire normal skeleton. This is followed by a stimulus to remineralization between the fourth and the eighth day in both regions. At the end of the eighth day this stimulus is lost and it was found that the apparent demineralization of the normal bones follows a curve opposite to that of the maximum mineral uptake at the fracture site; i.e., mineral deposition is elevated at the site of fracture with loss of mineral from the normal bones. The uptake and loss of  $Sr^{85}$  for both areas enter the normal range at about three weeks. Beyond this time the physiologic steps leading to firm union cannot be quantitated by this method.

One figure.

CARL KAPLAN, M.D.  
University of Pennsylvania

## RADIATION EFFECTS

**Leukemia in Children Exposed to Ionizing Radiation.** Robert Murray, Philip Heckel, and Louis H. Hempelmann. *New England J. Med.* 261: 585-589, Sept. 17, 1959. (University of Rochester School of Medicine, Rochester, N. Y.)

Names of 6,473 children in Monroe County, New York, given x-ray therapy since 1930 were checked against the New York State Department of Health Cancer Registry to determine the incidence of leukemia occurring in this irradiated population. The irradiated group represented about one-fortieth of the children born in the county.

In agreement with previous investigations, the incidence of leukemia was found to be higher among irradiated than among nonirradiated children. There were 8 deaths from leukemia, all among those receiving so called "deep" therapy for enlarged thymus, pertussis, and lymphoid hyperplasia. No leukemic death occurred in some 2,400 who had been treated for such skin lesions as hemangioma. The probability of these 8 deaths occurring on a chance basis in a group in which 2 leukemic deaths would normally be expected is less than 1 in 1,000.

Conversely, a retrospective study of leukemic children in Monroe County was conducted to determine

prenatal and postnatal exposure. Interviews were obtained for 65 of the 75 children dying of leukemia between 1940 and 1957. Identical interviews were conducted with parents of 65 control children dying of non-malignant causes. In addition, parents in both groups were asked the same questions about 2 siblings nearest in age to the study child. It was found that exposure of leukemic children to the x-ray sources investigated versus the exposure of matched deceased controls and living siblings was higher only for so called "deep" x-ray therapy.

Prenatal exposure was not found to be high in the small sample of cases of leukemia. However, siblings of leukemic children had received slightly more than twice as much fetal irradiation as was found in sampling the entire county. This suggests that, when all pregnancies are considered, mothers of the leukemic children in Monroe County experienced more complications necessitating radiologic procedures than did the control mothers. There were insufficient cases to permit statistical analysis of the interval between radiation exposure and onset of leukemia.

One graph; 2 tables.

CHARLES M. GREENWALD, M.D.  
St. Cloud, Minn.

**Radium in Human Bone: The Dose in Microscopic Volumes of Bone.** R. E. Rowland and J. H. Marshall. *Radiation Res.* 11: 299-313, September 1959. (Radiological Physics Division, Argonne National Laboratory, Lemont, Ill.)

In order to gain a more complete understanding of the role of radiation dose in chronic radium toxicity, a quantitative study was made of the distribution of  $Ra^{226}$  in microscopic volumes of bone. For this purpose bone from persons who acquired radium either therapeutically or through industrial exposure and carried it for at least twenty years was examined. The technique employed was that of quantitative  $\alpha$ -track autoradiography. The distributions are expressed as terminal dose rates, in units of rads per day.

The activity in the diffuse distribution of radium was found to be relatively uniform in cortical bone. The average magnitude of this activity is about one-half of the hypothetical uniform distribution, i.e., the body burden divided by the bone weight.

The specific activities found in the hotspots, characterized by intense concentrations of radium, were, on the average, ninety times as great as that in the diffuse distribution, or thus about forty-five times as great as a hypothetical uniform distribution.

From a calculated blood curve, constructed to describe the disappearance of  $Ra^{226}$  from the blood of those patients who received equal weekly injections of  $RaCl_2$ , it was possible to predict the specific activity at which the hotspots were formed. Since the terminal activities are less than one-tenth this value, the authors assume that a long-term exchange process may have removed nine-tenths of the original activity over a twenty-six-year period.

Three figures; 5 tables.

**Observations on the Dose from Dental X-Ray Procedures, with a Note on Radiography of the Nasal Bones.** G. M. Ardran and H. E. Crooks. *Brit. J. Radiol.* 32: 572-583, September 1959. (X-Ray Department, Medical Division, A. E. R. E., Harwell, England)

The basic principles of x-ray protection involved in dental radiography are again outlined and discussed. A comparison is made between the traditional plastic coned dental unit and a modern dental unit (the Watson "Kingsway" Unit) designed to obtain a small skin dose, gonadal dose, and integral dose to the patient. The "Kingsway" unit incorporates heavier tube shielding, built-in filtration, and a choice of a 2-inch-diameter (8 1/2-inch F.S.D.) or a 1-inch-diameter (10 1/2-inch F.S.D.) brass tube cone. The superiority of this machine over the traditional models is self-evident.

The authors suggest that the present British radiation limits for leakage of diagnostic tube housing (100 mr per hour at a distance of 1 meter, identical with those in the N.B.S. *Handbook 60*) are probably too liberal for dental units. This type of radiation, they believe, contributes significantly to the gonadal dose in routine dental radiography.

A comparison of the diagnostic quality and relative speeds of the commonly available dental film and screen film combinations, and critical examination of dental darkroom technique are included.

This article is an exhaustive coverage of the subject and deserves the attention of all dental radiographers and designers of dental x-ray units. Reference is made to the study by Gorson *et al.* on this subject (*Radiology*

72: 1, 1959) and their recommendations are endorsed. Nine figures; 8 tables.

JOSEPH E. WHITLEY, M.D.  
Bowman Gray School of Medicine

**Injury and Repair Following Irradiation of Salivary Glands in Male Rats.** C. P. Cherry and A. Glucksmann. *Brit. J. Radiol.* 32: 596-608, September 1959. (Strangeways Research Laboratory, Cambridge, England)

Local roentgen irradiation was given to the salivary glands of rats with the aim of studying the processes of injury and regeneration with particular reference to the effect on differentiation of the regenerating glands. In most of the rats 850 r daily was delivered to the gland region for four consecutive days at 200 kv, and the salivary glands were removed for study at intervals from one hour to one year. A temporary decrease in gland size and weight during the first month was followed by a second decrease beginning at about five months. This sequence paralleled the microscopic findings of a critical period (three months) of predominantly degenerative changes followed by a phase of regeneration and repair (fourth and fifth months). In all 3 glands the acini were affected most and the excretory tubules least. In the parotid, only the acini showed regenerative activity, and repair of the injury followed low (under 3,000 r) but not high doses of radiation. This "all-or-none" response is not observed in the submandibular and sublingual glands, in which partial and unsuccessful regeneration of acini elicits excessive proliferation of intercalated ducts, leading to the formation of adenomas. Whether malignant progression occurs in these adenomas is under investigation. The different response of the parotid may be linked with the higher mitotic index of its acini.

The differences in response of various glandular components in a given gland and from one gland to another are described, and the relation of the radiosensitivity of the various components to their mitotic and functional activities and to their regenerative pattern is discussed.

Twenty-one photomicrographs; 1 diagram; 3 tables.

WILLIAM A. COVELL, M.D.  
Bowman Gray School of Medicine

**Bone Marrow Transplantation and Chemical Protection in the Radiotherapy of Mouse Leukemia (Preliminary Communication).** Emanuel E. Schwartz. *Acta radiol.* 52: 235-240, September 1959. (Oak Ridge National Laboratory, Oak Ridge, Tenn.)

Measures that increase the tolerance to radiation constitute means of enhancing tumor therapy. The author attempted to extend the radiation-induced survival of mice, in which he had transplanted lymphomas, by using isologous bone marrow or the chemical protective agent AET. It was found that the mice receiving isologous bone marrow following irradiation could tolerate increased exposures and lived longer than those treated with sublethal doses of roentgen rays alone. The mice treated with AET could also tolerate increased amounts of radiation and one of 2 animals with transplanted lymphoma showed prolonged survival. The author also found that fractionated or protracted irradiation was not significantly more effective than a single exposure under the conditions tested.

EDWIN F. KOCH, JR., M.D.  
Indiana University Medical Center



**Autologous Bone-Marrow Implantation after Fast Neutron Irradiation of Dogs.** E. L. Alpen and S. J. Baum. *Radiation Res.* 11: 383-389, September 1959. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

Eleven dogs exposed to normally supralethal doses of neutrons (470 rads) produced by the  ${}^4\text{Be}(\alpha,n){}^7\text{B}$  reaction at the 60-inch Crocker Laboratory cyclotron were injected with autologous bone marrow collected before radiation exposure. Injection of  $1$  to  $2 \times 10^9$  nucleated cells immediately after radiation provided protection adequate for the survival of 7 out of the 11 exposed animals. The other 4 dogs died a characteristic "gastrointestinal" death with a survival time of 3.7 days; this finding provides strong additional evidence for a suggested high effectiveness of neutron radiation on gut tissues.

Hematological studies indicate that reimplanted marrow grows successfully after irradiation with neutrons and supports previous observations in the authors' laboratory that dogs can be provided with hematological protection after x-ray doses as high as 600 r (Alpen and Baum: *Blood* 13: 1168, 1958. *Abst. in Radiology* 73: 669, 1959).

Three figures; 1 table.

**Effects of Dose-Rate and Protraction: A Symposium. I. Patterns of Response to Whole-Body Irradiation: The Effect of Dose Intensity and Exposure Time on Duration of Life and Tumour Production.** R. H. Mole. *Brit. J. Radiol.* 32: 497-501, August 1959. (Medical Research Council Radiobiological Research Unit, Harwell, Didcot, Berks., England)

**II. Adaptation to Continuous Irradiation: Observations on the Rat Intestine.** H. Quastler, J. P. M. Bensted, L. F. Lamerton, and S. M. Simpson. *Brit. J. Radiol.* 32: 501-512, August 1959. (J. P. M. B., Royal Cancer Hospital, London, S. W. 3, England)

**III. Problems of Injury and Repair in Tissues and Cells: A Review.** G. Payling Wright. *Brit. J. Radiol.* 32: 512-516, August 1959. (Guy's Hospital Medical School, London, S. E. 1, England)

The three papers listed above were presented as a Symposium at the Annual Congress of the British Institute of Radiology in December 1958.

Mole opens the Symposium with the statement that "there seems to be a basic difference of approach between those who are trying to improve radiotherapy and those who are trying to understand the ways in which unwanted exposure to radiation can lead to harm." The aim of the therapist is often to destroy something selectively, and what matters is how completely the pathological lesion can be eradicated. Of fundamental importance are the mechanisms by which radiation kills cells or prevents their further division. When considering the harmful effect of unwanted irradiation, however, it is not of primary importance what the mechanisms of cell death or of interference with cell division are, or how many cells are so affected,

provided that some cells survive and can multiply to replace those that are missing.

Many of the effects produced by daily irradiation depend on a balance between daily depletion and daily replacement of cells. During the initial stages of the radiation exposure a degree of damage develops but with continued exposure the damage, instead of progressively increasing, appears to reach a steady state, at least for a time. This occurs for only a small range of daily dose, about four- to eight-fold, the damage ranging from barely measurable to gross. (With daily doses larger than this, the damage progressively increases to complete functional failure.) These effects are independent of dose-intensity during irradiation, radiation-free time between the individual exposures, and LET (linear energy transfer). Increasing the overall time in which a fixed total dose is given always reduces the effect.

A contrasting pattern of response is found in delayed lethal radiation damage in mice. The degree of life shortening depends on the incidence of leukemia. For this type of response, increasing the overall time increases the effect of a fixed dose, and dose-intensity of the individual radiation exposures may be quantitatively important.

Four figures; 1 table.

Quastler and his associates describe an experiment in which male rats received continuous whole-body irradiation at dose rates of 84, 176, and 415 rads per day. Radiation injury appeared soon in the intestinal crypts and villi, but was not progressive. A steady state developed at each dose rate. Since it is known that irradiation can induce increased ploidy, and that this is sometimes accompanied by an increase in radioresistance, it is possible that this is the mechanism of adaptation, as has been suggested by Sparrow (1958).

Thirty-four photomicrographs; 2 diagrams; 1 graphs; 2 tables.

Wright points out that, unless the damage is so severe, animal cells respond to injury with a reparative reaction. If given time to recover fully, they can endure with success a second assault, but before repair is complete they will be more vulnerable. They may also attain some incomplete stage in repair and halt there, sometimes appearing more susceptible and sometimes more resistant to a second assault. An example of the latter phenomenon is repeated smallpox vaccination.

If polyploid cells are more radioresistant, irradiation might lead to a differential mortality between the normal diploid and the polyploid cells. Thus, the intestinal epithelium might be repopulated by less vulnerable cells.

It is not, however, necessary to postulate that the epithelium has undergone any selectively raised resistance. Many substances which are lethal when administered rapidly are tolerated if the dose rate is low.

LUCILLE DU SAULT  
The Henry Ford Hospital



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